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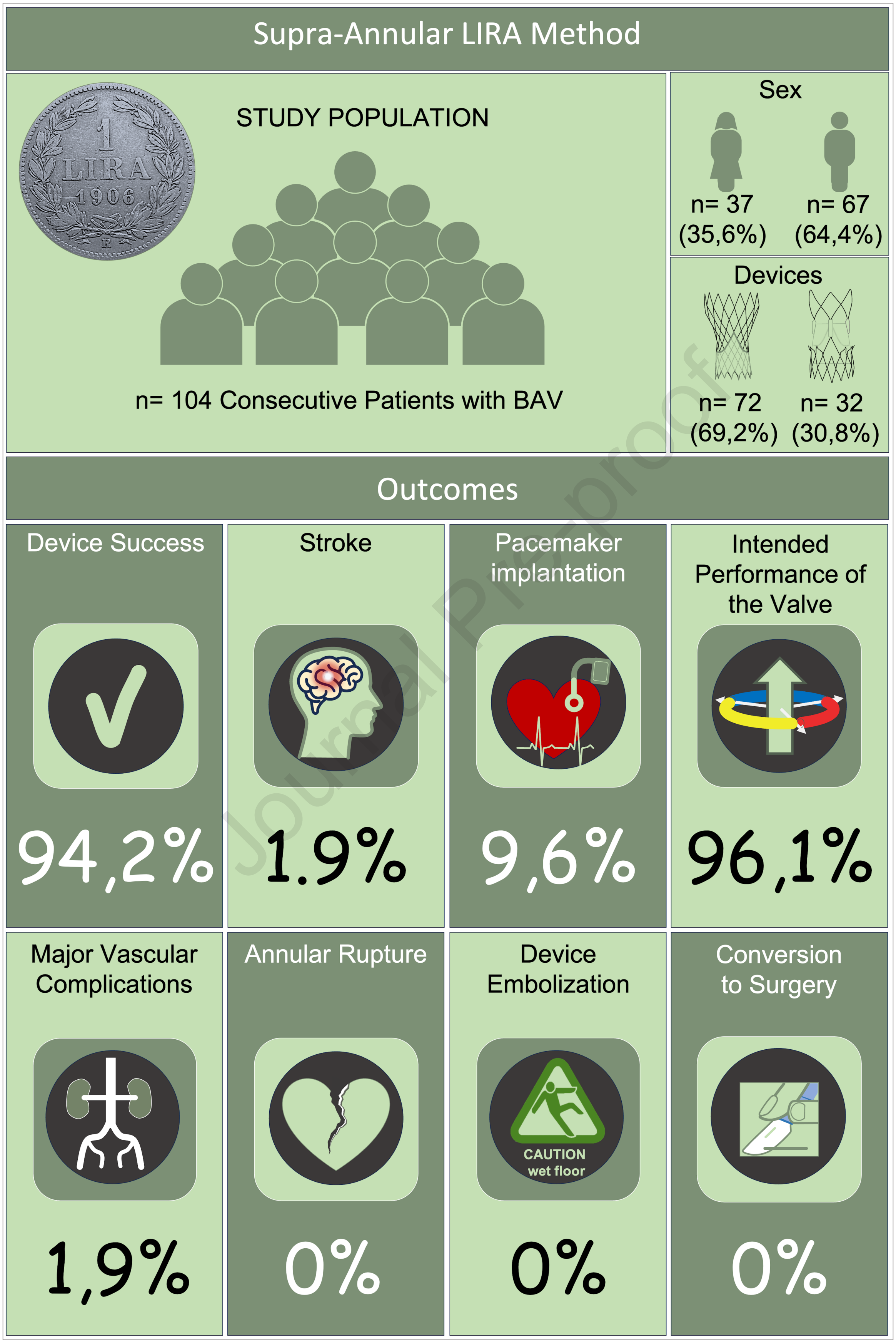
Supra-Annular LIRA Method
1 LIRA 1906
STUDY POPULATION
n= 104 Consecutive Patients with BAV
Sex
n= 37 (35,6%)
n= 67 (64,4%)
Devices
n= 72 (69,2%)
n= 32 (30,8%)
Outcomes
Device Success
94,2%
Stroke
1.9%
Pacemaker implantation
9,6%
Intended Performance of the Valve
96,1%
Major Vascular Complications
1,9%
Annular Rupture
0%
Device Embolization
CAUTION wet floor
0%
Conversion to Surgery
0%

Clinical outcomes of patients with bicuspid aortic valve undergoing a targeted transcatheter aortic valve replacement approach: the LIRA Method

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Short title: *The LIRA method in BAV patients undergoing TAVR*

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Abstract

Background:

Transcatheter aortic valve replacement (TAVR) in patients with bicuspid aortic valve (BAV) disease is still burdened by a non-negligible rate of stroke and permanent pacemaker implantation (PPI). These suboptimal results, possibly related to the unique BAV anatomy, might suggest the use of a different sizing method in this setting.

The aim of our study is to evaluate whether the application of the supra-annular LIRA method might improve clinical outcomes in this population.

Methods:

In this single center retrospective study, we enrolled consecutive patients with severe aortic stenosis and raphe-type BAV undergone TAVR with the implantation of supra-annular self-expanding prostheses sized according to the LIRA method. The primary endpoint was the device success. Secondary endpoints were in-hospital and 30-days safety outcomes and 1-year clinical efficacy. All study endpoints were adjudicated according to VARC 3 criteria.

Results:

A total of 104 patients (mean age 79.8± 5.83) were enrolled in our study. Mean STS score was 4.96±4.73%. The use of the LIRA method led to prosthesis downsizing in 85.6% of patients.

Device success was 94.2%. All cause death was 0%, conversion to surgery was 0% and an extremely low rate of stroke (1.9%) and PPI (9.6%) was observed.

The intended performance of the valve was 96.1% and it was maintained at 1-year follow-up. Clinical efficacy at 1-year was reached in 90.6% of patients.

Conclusions:

The LIRA method represents an alternative option for prosthesis sizing in patients with type 1 and type 2 BAV undergoing TAVR with promising early and mid-term outcomes.

Key words: aortic stenosis, bicuspid aortic valve, raphe, transcatheter aortic valve replacement

Abbreviations and Acronyms:

AV: Atrioventricular

BAV: Bicuspid aortic valve

BEV: Balloon Expandable Valve

CT: Computed Tomography

ECG: Electrocardiogram

ICD: Intercommissural distance

LIRA: Level of Implantation at the RAphe

L-R: Left-Right

LVOT: Left ventricular outflow tract

MDCT: Multidetector Computed Tomography

PPI: Permanent Pacemaker Implantation

PVL: Paravalvular leak

SD: Standard deviation

SEV: Self-Expanding Valve

STS: Society of Thoracic Surgeons Score

TAVR: Transcatheter aortic valve replacement

THV: Transcatheter heart valve

TVT: Transcatheter Valve Therapy

VARC: Valve Academic Research Consortium

VBR: Virtual basal ring

Introduction

Bicuspid aortic valve (BAV) disease still represents a challenge for percutaneous treatment due to the unique anatomy.

BAV patients have historically been excluded from major randomized controlled trials, so that available evidence arises mostly from observational studies.

Previous registries (1-6) have showed a high rate of paravalvular leaks (PVL) with the use of self-expanding valves (SEV) and a non-negligible rate of annular rupture with the use of balloon expandable valves (BEV).

Although more recent studies (7-8) have shown better outcomes with current generation prostheses, the rate of stroke (9-10) and permanent pacemaker implantation (10) is still high and some characteristics such as calcified raphe and excessive leaflet calcification have been associated to increased procedural complications and higher mid-term mortality (11).

These suboptimal results, possibly related to the unique anatomic features of bicuspid disease, may advocate the use of a different sizing method in this setting.

In patients with tricuspid anatomy transcatheter heart valve (THV) anchoring and sealing occurs at the level of the virtual basal ring (VBR), so that the sizing of THV is based on the measurement of the perimeter (for self-expanding prostheses) and the area (for balloon expandable prostheses) performed at this level.

Conversely in BAV patients THV anchoring might occur at the raphe-level, that we defined as the LIRA (Level of Implantation at the RAphe) plane. Indeed, we found a precise correspondence between the prosthesis waist height measured at Computed Tomography (CT) scan performed after transcatheter aortic valve replacement (TAVR) and the height of the LIRA plane (12).

Thus, we developed a novel supra-annular sizing method based on the measurement of the perimeter at this level, the LIRA-method, that has already been validated in small cohorts of patients (13-15).

In this study we report the early and mid-term outcomes of the application of the LIRA method in patients with raphe-type BAV undergoing TAVR.

Material and methods

Study population

In this retrospective single center study, we enrolled all consecutive patients with type 1 and type 2 bicuspid anatomy defined according to Sievers Classification (16) that underwent TAVR for native severe aortic stenosis between September 2018 and June 2024 at the authors' center.

All patients underwent the implantation of a supra-annular self-expanding THV sized according to the LIRA method.

Patients with type 0 bicuspid anatomy, previous aortic intervention and TAVR performed in emergency setting or for pure aortic regurgitation were excluded.

All patients were scheduled for TAVR after Heart Team discussion.

The study was approved by the local Institutional Review Board and conducted in accordance with the Declaration of Helsinki.

The LIRA Method

The key concept of the LIRA method (12-13) is to consider the role of the raphe in prosthesis anchoring and deployment. Indeed, the raphe is a rigid structure that might represent the point of maximal constraint across the aortic valvar complex allowing prosthesis anchoring and might affect the deployment of the THV, pushing the prosthesis in the opposite direction of the conjoint cusp.

As previously described (13), the LIRA method consists in the measurement of the perimeter at the level of the maximal protrusion of the raphe (the LIRA plane) obtained tracing the internal borders of the leaflets excluding all the structures encountered at this level (**Figure 1).** Even the perimeter at the level of the virtual basal ring is analyzed and in case of discrepancy between the two measures, the smallest value is chosen for prosthesis sizing.

We defined as tapered anatomy of the aortic valvar complex (**Figure 2**) the presence of a perimeter at LIRA plane smaller than the perimeter measured at VBR.

Data collection and clinical endpoints

Clinical and electrocardiographic characteristics as well as imaging and procedural data were collected in a dedicated anonymized dataset.

Echocardiographic assessments were performed by expert board certified operators according to current recommendations.

All patients underwent pre-operative Electrocardiogram (ECG)-gated Multidetector Computed Tomography (MDCT) assessment for procedural planning.

The images were then analyzed using the software OsiriX DICOM viewer, with three-dimensional and multi-planar sections, evaluating VBR perimeter, type of bicuspid valve, raphe length, raphe calcification, distance between the LIRA plane and the virtual basal ring, LIRA plane perimeter, inter-commissural distance (ICD) at 4 mm and at the LIRA plane, calcification of the left ventricular outflow tract (LVOT) and ascending aorta diameter.

CT scan analyses were performed by two expert operators (M.M. and V.R.).

Clinical outcomes and echocardiographic evaluations were collected at discharge, at 30-days and at 1 year.

The primary endpoint was the device success at 30-days, a composite endpoint including:

• Technical success

• Freedom from mortality

• Freedom from surgery or intervention related to the device, or to a major vascular or access-related or cardiac structural complication

• Intended performance of the valve defined as mean gradient <20 mmHg, peak velocity <3 m/s, and less than moderate aortic regurgitation.

Secondary endpoints were in-hospital and 30-days safety outcomes and 1-year clinical efficacy, defined as freedom from all-cause mortality, freedom from all stroke, and freedom from hospitalization for procedure- or valve-related causes.

All study endpoints were adjudicated according to the Valve Academic Research Consortium 3 (VARC 3) criteria (17).

Statistical Analysis

Categorical variables were presented as number (percentages) of patients.

For continuous variables, normality of the distribution was evaluated using the Kolmogorov-Smirnov test. Normally distributed continuous variables were expressed as mean±standard deviation; non-normally distributed continuous variables were presented as median and inter-quartile range (IQR, 25th-75th percentile).

A paired t-test was used to test for differences in means with continuous variables, and a two-sided P- value <0.05 was considered statistically significant.

All analyses were performed using SPSS (Chicago, Illinois).

Results

Study population and CT scan findings

A total of 104 patients (mean age 79.8± 5.83; 64.4% males) were enrolled in our study. Mean Society of Thoracic Surgeons (STS) score was 4.96±4.73%. 80.8% (n=84) of patients had hypertension, 20.2% (n=21) had diabetes and 37.5% (n=39) of patients had history of coronary artery disease. Noteworthy, 6.7 % (n=7) of patients had history of previous stroke, while 7.7% (n=8) of patients had a pre-existing right-bundle branch block. Baseline clinical and electrocardiographic characteristics are reported in **Table 1**.

Mean ejection fraction was 54.91±11.70%, while mean transaortic gradient was 47 ± 12.47 mmHg. Type I Left-Right (L-R) BAV was observed in 76% (n=79) of patients. A calcific raphe was found in 84.6% (n=88) of patients, while LVOT calcification were observed in 35.6 % (n=37) of patients.

ICD at 4 mm was measurable in 39 (37.5%) of patients, with a mean value of 27.51 ± 13.52 mm.

The mean distance of the LIRA plane from the virtual basal ring was 7.76±2.03 mm.

The VBR perimeter was significantly larger than the LIRA plane perimeter (81.74 ± 11.23 vs 72.32 ± 7.74; P<0.001).

The application of the LIRA method led to prosthesis downsizing in 85.6% of patients.

Echocardiographic and CT scan findings are summarized in **Table 2**.

Procedural characteristics

All patients underwent supra-annular self-expanding THV implantation. Predilatation was performed in 92.3% (n=96) of patients, while in 26.9% (n=28) of cases a post-dilatation was required to optimize TAVR results. Procedural characteristics are represented in **Table 3**.

In-hospital and 30-days outcomes

Device success was obtained in 94.2% (n=98) of cases. Reasons for not achieving device success were moderate PVL in 4 patients and technical failure with a major access-related complication in 2 patients. In one patient the failure of the closure device resulted in a VARC type 2 bleeding and formation of a pseudoaneurysm successfully treated by surgical repair. In the second patient a VARC type 2 bleeding occurred with need for covered stent implantation.

The intended performance of the valve was 96.1% (n=100), while the mean aortic gradient was 9 ± 2.93 mmHg.

Regarding the safety endpoints all cause death was 0%, conversion to surgery was 0% , embolization was 0%, the rate of major vascular complications was 1.9% (n=2) and a low rate of stroke (1.9%; n=2), none of them being disabling, and permanent pacemaker implantation (9.6%; n=10) was observed.

In-hospital and 30-days outcomes are reported in **Table 4**.

1-year outcomes

At 1-year all-cause death was 6.2% (n=6), cardiovascular death was 0%, and the rate of stroke was 3.1% (n=3). No hospitalization for procedural or valve-related causes was reported and the intended performance of the valve was maintained (94.9%; n=74). Clinical efficacy was reached in 90.6% (n=87) of patients.

1-year outcomes are summarized in **Table 5.**

Discussion

The main findings of our study are as follows:

1. The LIRA method showed a high efficacy (technical and device success >94% and good intended performance of the valve at 30 days follow-up).
2. The LIRA method displayed an excellent safety profile (no all cause-death, no conversion to surgery, no embolization, extremely low-rate of stroke and permanent pacemaker implantation at 30-days).
3. One-year outcomes are promising.

The unique anatomical features of BAV disease and the suboptimal results of TAVR with the application of the traditional annular method have encouraged the development of alternative, dedicated sizing methods.

In the BAVARD (Bicuspid Aortic Valve Anatomy and Relationship with Devices) Registry (18) Tchetche at al compared prostheses geometry analyzed at CT scan performed post-TAVR in bicuspid vs tricuspid patients. The main finding was the underexpansion of the THV observed in BAV patients, underscoring the presence of potential points of constraint across the aortic root. For this reason, the authors speculated that similarly to tricuspid anatomy in which the landing zone of a THV is located up to 4 mm below the VBR (in the LVOT), in BAV anatomy the landing zone might be located up to 4 mm above the VBR. Thus, they suggested considering the intercommissural distance (ICD) at 4 mm as an adjunctive parameter for prosthesis sizing in BAV patients, at least in patients with tapered anatomy of the aortic valvar complex (ICD smaller than the mean perimeter-derived diameter). Noteworthy, in this study a tapered anatomy was found only in a minority of patients (less than 12%).

However, it is known that the point of constraint of the prosthesis, the raphe level (LIRA plane) is not located at a fixed distance (12) but varies from patient to patient: in our population the mean distance of the LIRA plane from the virtual basal ring was 7.76±2.03

mm, indeed in 62.5% of patients at 4 mm the raphe was not displayed, so it was impossible to measure the ICD at that level.

In our population a tapered anatomy (**Figure 2**), that we defined as the presence of a perimeter at the LIRA plane smaller than the perimeter measured at the virtual basal ring, was the most frequent configuration. Indeed in 72.1% of cases the LIRA method led to the choice of one size smaller prosthesis, while in 13.5% a prosthesis of two sizes smaller was implanted. Noteworthy, the downsizing is determined by the perimeter at the LIRA plane (**Figure 3**), independently of the characteristics of the raphe (calcific or fibrotic).

The LIRA method showed an excellent efficacy with a high rate of both technical (98.1%) and device success (94.2%) and a good intended performance of the valve (96.1%). These results are comparable to the ones reported by the most recent bicuspid trials. Indeed, the Bivolut X Registry reported a device success of 91.3% and an intended performance of the valve at 30 days of 95.3% (10). A similar performance of the valve was observed in the Medtronic Low risk bicuspid study (19).

The excellent valve hemodynamic observed in these studies might be explained by the supra-annular design that counterbalances the risk of prosthesis underexpansion at the level of the raphe, ensuring low prosthetic gradients even in the presence of an elliptical shape of the frame at the raphe level. Indeed, even in our population the mean post-procedural gradient was low (9 ± 2.93 mmHg) and it was stable at 1-year follow-up.

In our study no patient experienced more than moderate PVL. Of note, only in a minority of patients (21.15%) the prosthesis implanted had a sealing skirt and none of them showed significant PVL. This finding might suggest that the use of current generation prostheses (Acurate Neo 2, Boston Scientific; CoreValve Evolut Pro, Pro + and Fx, Medtronic) might reduce even more the PVL rate. Our data are consistent with the large analysis from the

Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy (TVT) registry comparing the outcomes of 929 bicuspid patients with a propensity matched group of tricuspid patients (20). In this study the use of SEV led to low post-procedural gradients (mean 9 mmHg±5.2 mmHg) both in bicuspid and in tricuspid patients, but a higher rate of moderate-or-severe PVL was observed in the bicuspid cohort (5.6% vs. 2.1; p <0.001). Interestingly, this difference was not significant (2.1 vs 1.5; p=0.70) when only patients implanted with the Evolut Pro device were analyzed, underlying the importance of the pericardial wrap to reduce the PVL rate.

Moreover, in our study safety outcomes were particularly promising: there was no all cause death at discharge and at 1 month follow-up, no annular rupture, conversion to surgery or embolization and there was a remarkably low rate of stroke and permanent pacemaker implantation.

It is well known that BAV disease might be a marker of aortopathy. Pre-TAVR CT scan might underline the presence of aortic dilatation but so far there is no diagnostic tool to assess the vulnerability of the aortic walls. A sub-analysis of the BEAT (Balloon versus Self-Expandable valves for Treatment of bicuspid Aortic valve sTenosis) Registry (6) comparing the performance of new generation SEV vs BEV in a cohort of 353 patients showed a non-negligible rate of annular rupture (1.7%) with the use of BEV, while no such complication was observed with SEV. Indeed, the attempt to circularize an elliptic anatomy with the risk of excessive oversizing might result in this catastrophic complication.

In the analysis from the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy (TVT) Registry comparing the outcomes of patients implanted with BEV in bicuspid vs tricuspid anatomy (21) the authors report a similar mortality between the two groups but the rate of complications requiring open surgery was significantly higher in the bicuspid cohort.

The use of undersized SEV, being more respectful of the bicuspid anatomy and geometry, might reduce the risk of such events.

Furthermore, we report an overall rate of stroke at 30-days of 1.9% and a rate of disabling stroke of 0%. These data are more favorable than the one reported in other contemporary SEV trials (4% in the Medtronic low risk trial and 4.6% in the Bivolut X Registry). These results are even more striking considering that our population was at intermediate risk (mean STS score of 4.9%) and that 6.7% of patients experienced a previous cerebrovascular accident. Moreover, in most patients we found a calcific raphe (84.6%), a well know marker of increased procedural complications (11). We speculate that predilatation with undersized balloons (sized according to the LIRA-perimeter derived diameter) might contribute to reduce the risk of peri-procedural stroke.

Finally, we observed a low rate of pacemaker implantation (9.6%), only in a minority of cases (6 patients) related to 3rd-degree atrioventricular (AV) block.

Noteworthy in 17.3% of patients a big prosthesis size (Corevalve Evolut 34 mm or Acurate L) was implanted, 7.7% of patients had a pre-existing right bundle branch block, a well known predictor of permanent pacemaker implantation (PPI), and the cusp overlap technique was not available in the early phase of our study.

A previous multicenter registry by Perlman et al. (22) evaluated the results of Sapien 3 implantation in a bicuspid cohort of 51 patients. They report a good valve performance but at cost of a very high PPI rate at 30-days (23.5%). Contemporary reports about SEV did not perform better: indeed, the Evolut Low risk trial (19) observed a 30-days PPI rate of 15% while in the Bivolut X Registry (10) the 30-days PPI rate was of 19%.

Our single-digit rate of PPI might be explained by the fact that the undersized SEV will anchor at the raphe level with minimal interaction of the prosthesis frame with the membranous septum (**Figure 4**).

Study limitations

The results of this study should be interpreted in the light of some limitations:

- The LIRA sizing method, being based on the measurement of a perimeter, does not apply to BEV. Self-expanding prostheses adapt to patient's anatomy without causing a circularization of the elliptic bicuspid annulus, as balloon expandable prostheses do. This is the reason why in our belief SEV are less traumatic in the setting of BAV disease, where a concomitant aortopathy may coexist. Moreover, the presence of the raphe might hamper prosthesis expansion with unfavorable consequences in BEV (that have an intra-annular design). SEV with a supra-annular design, instead, even when not fully expanded at the level of the raphe, may maintain an adequate circularity at the coaptation level ensuring a good valve performance. For these reasons, our sizing method was specifically developed for SEV.
- Our study is a non-randomized, single-center study. This latter characteristic, on the other hand, ensured a homogeneous diagnostic and therapeutic approach.
- There was no core lab analysis for CT scan measurements and for echocardiographic assessment.
- The length of the follow-up was of only one year, so to analyze prosthesis durability, a longer follow-up is needed.

Conclusions

The application of the supra-annular LIRA method for prosthesis sizing in patients with type 1 and type 2 bicuspid anatomy undergoing TAVR achieved promising early and mid-term outcomes. As TAVR indication is expanding towards younger and lower risk patients, it is of paramount importance to achieve optimal procedural results in this population.

Data sharing:

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Disclosures:

Dr. M. Ancona received consultant fees from Abbott and Abiomed.

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Professor M. Montorfano received consultant fees from Abbott, Boston Scientific, Kardia and Medtronic.

Dr. F. Russo received consultant fees from Boston Scientific.

The other authors have nothing to declare.

The authors confirm that patients' consent forms have been obtained for this article.

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Table 1. Baseline clinical and electrocardiographic characteristics (N = 104 patients).

Age (years)	79.8 ± 5.83
Male sex	67 (64.4)
BMI (kg/m^2)	25.67 ± 4.07
STS score (%)	4.96 ± 4.73
Hypertension	84 (80.8)
Diabetes	21 (20.2)
eGFR	53.26 ± 18.20
eGFR < 45 ml/min/1.73m^2	33 (31.7)
Coronary artery disease	39 (37.5)
Previous stroke	7 (6.7)
Peripheral Vascular Disease	23 (22.1)
Syncope	14 (13.5)
NYHA III-IV	35 (33.6)
Atrial fibrillation	19 (18.3)
Right-bundle branch block	8 (7.7)
Left-bundle branch block	9 (8.6)
First degree heart block	13 (12.5)

Values are expressed as n/N of patients (%) or mean ± standard deviation.
BMI, body mass index; STS, Society of Thoracic Surgeons; eGFR, estimated glomerular filtration rate; NYHA, The New York Heart Association.

Table 2. Echocardiographic and CT scan findings (N = 104 patients)

Ejection fraction (%)	54.91 ± 11.70
Mean gradient (mmHg)	47 ± 12.47
Aortic valve area (cm^2)	0.77 ± 0.20
Stroke volume index (ml/m^2)	47.21 ± 17.04
Aortic valve regurgitation ≥ moderate	42 (40.4)
Mitral valve regurgitation ≥ moderate	29 (27.9)
Tricuspid valve regurgitation ≥ moderate	17 (16.3)
Type of bicuspid aortic valve	
Type 1	98 (94.2)
L-R	79 (76.0)
R-N	14 (13.5)
L-N	5 (4.8)
Type 2	6 (5.8)
L-N + R-N	3 (2.9)
L-R + L-N	1 (1.0)
L-R + R-N	2 (1.9)
Raphe characteristics	
Fibrotic raphe	16 (15.4)
Calcific raphe	88 (84.6)
Raphe length	11.55 ± 2.47
Calcium raphe length	6.90 ± 4.07
Distance LIRA plane-VBR	7.76 ± 2.03
VBR sizing	
$Diameter_{min}$	23.27 ± 2.37
$Diameter_{max}$	28.29 ± 3.17
Perimeter	81.74 ± 11.23
Eccentricity index	0.18 ± 0.09
LIRA plane sizing	
Perimeter	72.32 ± 7.74
Perimeter-derived diameter	23 ± 2.49
ICD	26.75 ± 4.86
ICD 4 mm above VBR (when 2 commissures visibles)*	27.51 ± 13.52
Calcium in LVOT	37 (35.6)
Sinotubular junction	30.33 ± 3.44
Ascending aorta	37.47 ± 4.60
Coronary artery height	
LMCA	13.22 ± 3.41
RCA	16.96 ± 4.18
Downsizing	89 (85.6)
Calcium score AU	2781.34 ± 1456.88
Calcium score mm^3	2848.84 ± 1430.18

Values are expressed as n/N of patients (%) or mean ± standard deviation. CT, computed tomography; L, left; R, right; N, non-coronary; VBR, virtual basal ring; LIRA, Level of Implantation at the RAphe; LMCA, left main coronary artery; LVOT, left ventricular out-flow tract; RCA, right coronary artery; ICD, intercommissural distance; AU, Agatston units. *ICD was measurable at 4 mm in 39 patients (37.5%).

Table 3. Procedural characteristics (N = 104 patients).

Corevalve Evolut R	66 (63.5)
23 mm	9
26 mm	22
29 mm	29
34 mm	6
Evolut Pro/Pro plus	2 (1.9)
29 mm	2
Evolut Fx	4 (3.8)
29 mm	1
34 mm	3
Acurate	16 (15.4)
S (23 mm)	7
M (25 mm)	4
L (27 mm)	5
Acurate Neo 2	16 (15.4)
S (23 mm)	6
M (25 mm)	6
L (27 mm)	4
Predilatation	96 (92.3)
Size (mm)	22 (20-22)
Postdilatation	28 (26.9)
Size (mm)	23 (21.5-24)
Cerebral protection	0 (0)

Values are expressed as n/N of patients (%) or median (IQR).

Table 4. In-hospital and 30-days outcomes.

In-hospital outcomes	**104 (100)**
Technical success	102 (98.1)
Intraprocedural death	0 (0)
Valve embolization	0 (0)
Coronary obstruction	0 (0)
Aortic injury	0 (0)
Annular rupture	0 (0)
Cardiac tamponade	0 (0)
Conversion to surgery	0 (0)
Myocardial infarction	0 (0)
30- days outcomes	**104 (100)**
Device success	98 (94.2)
Intended performance of the valve	100 (96.1)
All cause death	0 (0)
Stroke	2 (1.9)
VARC 2-4 bleedings	8 (7.6)
Major vascular complications	2 (1.9)
Acute kidney injury stage 3 or 4	2 (1.9)
Moderate or severe aortic regurgitation	4 (3.8)
Moderate PVL	4 (3.8)
Severe PVL	0 (0)
Permanent pacemaker implantation	10 (9.6)
Mean gradient > 20 mmHg	0 (0)
Mean gradient, mmHg	9 ± 2.93

Values are expressed as n/N of patients (%) or mean ± standard deviation. PVL=paravalvular leak.

Table 5. 1- year outcomes

Clinical outcomes	**96 (92.3)**
Clinical efficacy	87 (90.6)
Cardiovascular death	0 (0)
All-cause death	6 (6.2)
Stroke	3 (3.1)
Rehospitalization for procedure or valve-related causes	0 (0)
Echo follow-up	**78 (75)**
Mean gradient, mmHg	9.65 ± 3.25
Moderate or severe aortic regurgitation	3 (3.8)
Intended performance of the valve	74 (94.9)

Values are expressed as n/N of patients (%) or mean ± standard deviation.

Figure Legends

Figure 1. LIRA Method application.

Panel A. LIRA method in a patient with a protrudent raphe. On the left, sagittal view of the aortic valvar complex with the purple line cutting the point of maximal protrusion of the raphe (magnified view in the red circle). **Panel B.** On the left, sagittal view of the aortic valvar complex in a patient with a flat raphe (magnified view in the red circle). In this case the LIRA plane conventionally coincides with the axis cutting the raphe at 50%. On the right in Panel A and B: I. Transverse axis at the level of the raphe (LIRA plane); II. LIRA plane perimeter; III. Virtual basal ring perimeter; IV. CT scan post TAVR, sagittal view; V. Post-procedural prosthesis perimeter at the LIRA plane (note the correspondence with the LIRA plane perimeter); VI. Prosthesis frame at the level of the VBR.

Figure 2. Example of tapered configuration.

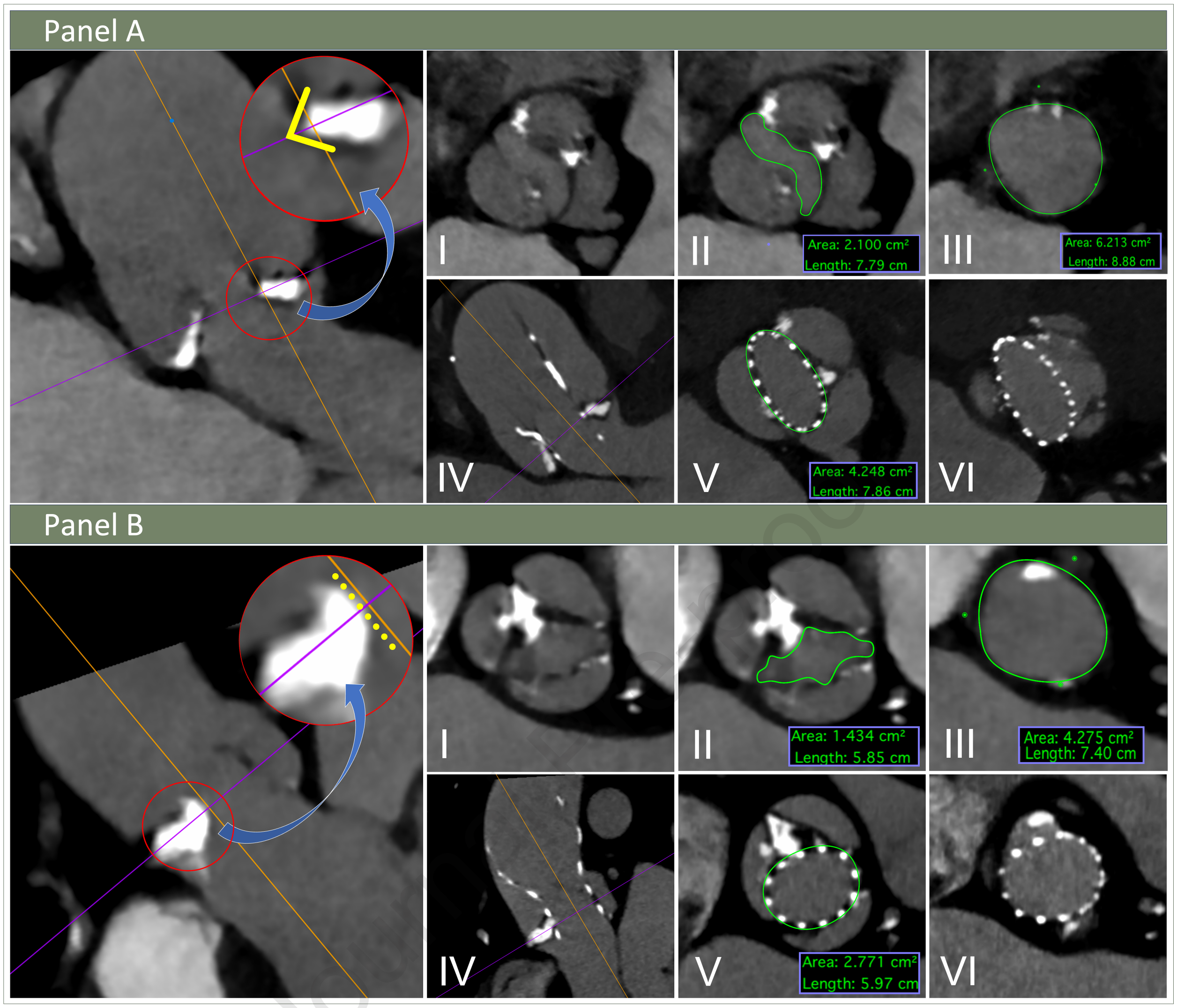
On the left, sagittal view of the aortic valvar complex. On the right, the typical volcano shape of the tapered configuration is displayed with the VBR perimeter (green circle) bigger than LIRA perimeter (yellow circle). AVA is delimited by the white circle on the top.

Figure 3. Examples of the application of the LIRA method in different anatomies.

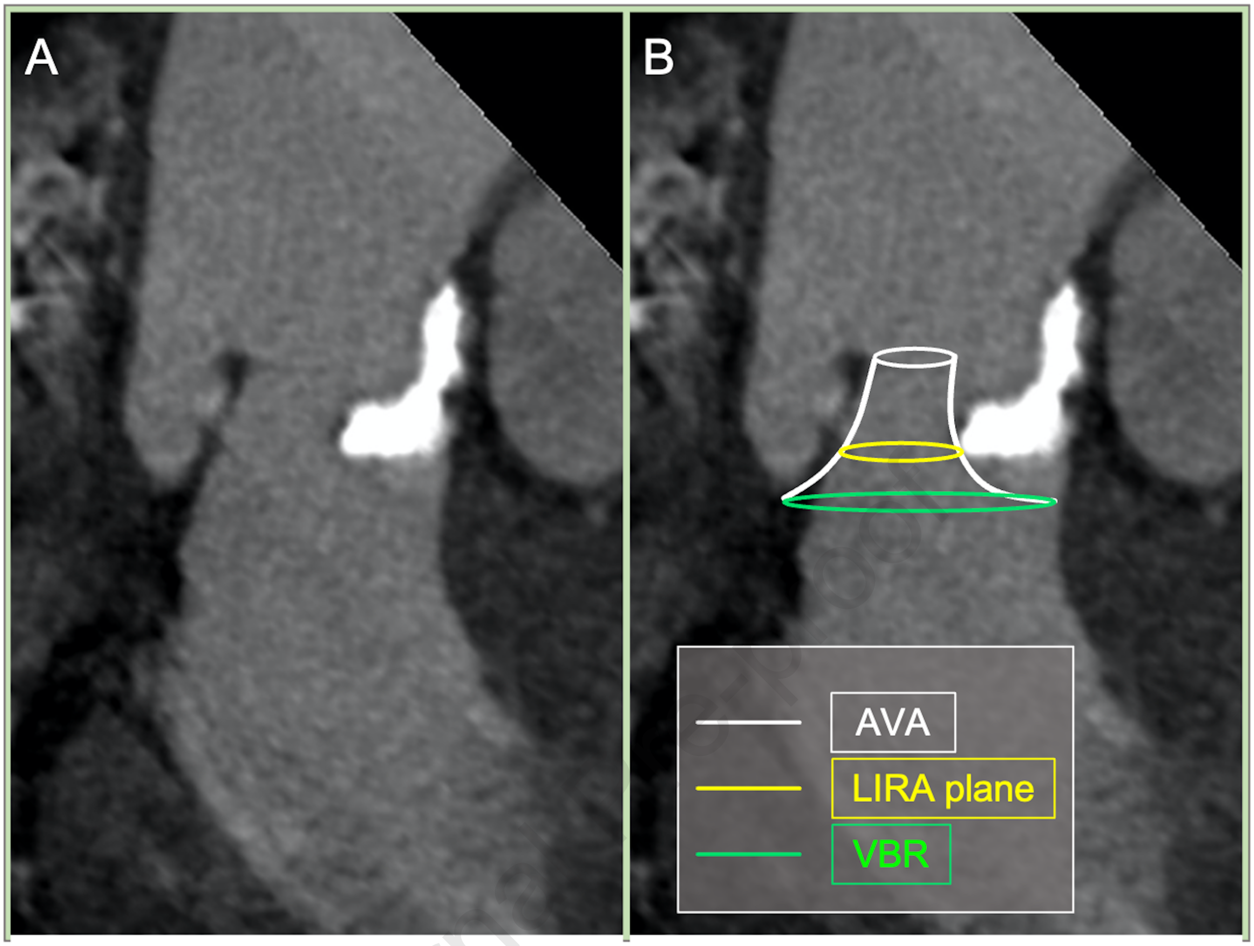
Panel A. Fibrotic raphe. **Panel B.** Fibrocalcific raphe. **Panel C.** Calcific raphe. **Panel D.** Extensive calcification (raphe and leaflets). I. Transverse axis at the LIRA plane. II. LIRA plane perimeter. III. Post-procedural prosthesis perimeter. Noteworthy, even in a fibrotic raphe the prosthesis is pushed away from the conjoint cusp.

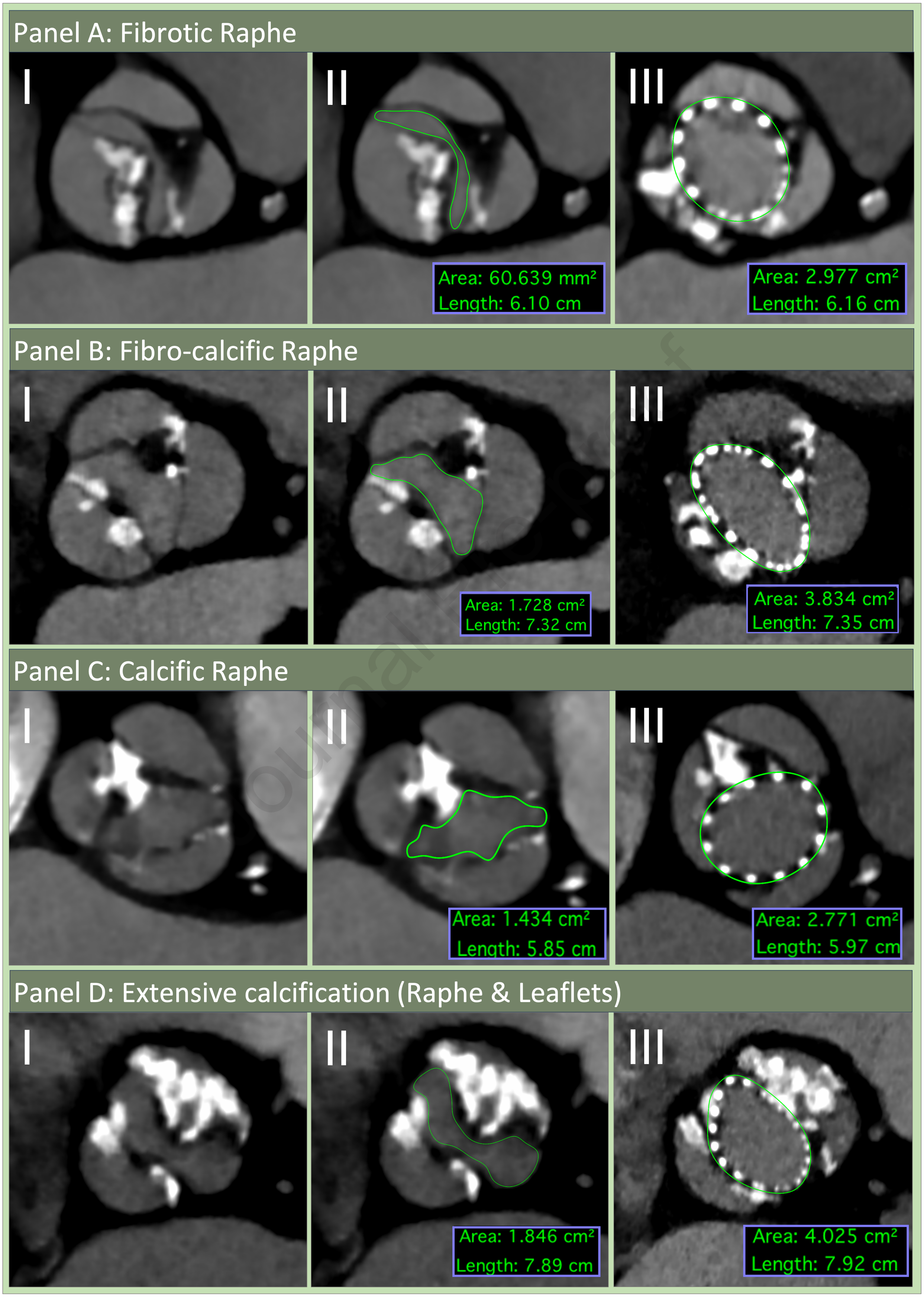
Figure 4. Post-TAVR CT scan in a patient with Corevalve Evolut R (**Panel A**) and Acurate Neo 2 (**Panel B**) sized according to the LIRA method.

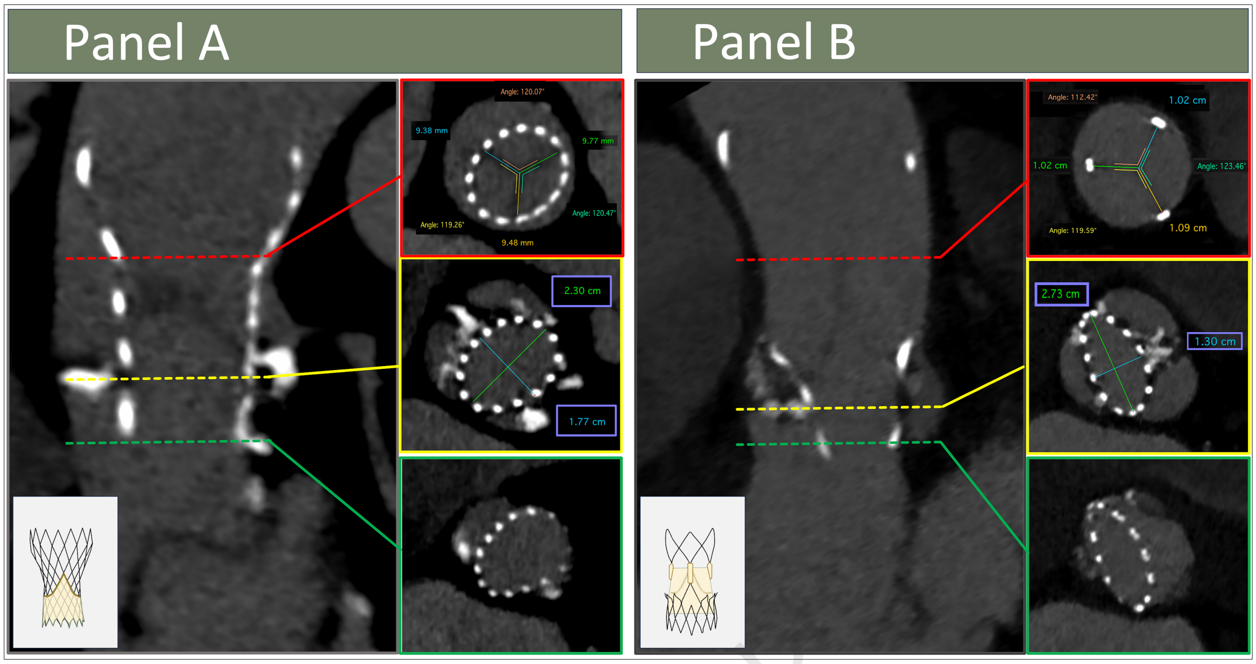
The red dotted line is drawn at the level of the leaflets' coaptation. Note the circularity of the prosthesis that is maintained at this level (red square). The yellow dotted line is drawn at the level of the raphe. Note the elliptical shape of the prosthesis frame at this level, without any distortion of the bicuspid geometry (yellow square). The green dotted line is drawn at the virtual basal ring level. Note the poor interaction of the prosthesis frame with the membranous septum (green square).



Panel A
I
II
Area: 2.100 cm²
Length: 7.79 cm
III
Area: 6.213 cm²
Length: 8.88 cm
IV
V
Area: 4.248 cm²
Length: 7.86 cm
VI
Panel B
I
II
Area: 1.434 cm²
Length: 5.85 cm
III
Area: 4.275 cm²
Length: 7.40 cm
IV
V
Area: 2.771 cm²
Length: 5.97 cm
VI


A
B
AVA
LIRA plane
VBR


Panel A: Fibrotic Raphe
I
II
Area: 60.639 mm²
Length: 6.10 cm
III
Area: 2.977 cm²
Length: 6.16 cm
Panel B: Fibro-calcific Raphe
I
II
Area: 1.728 cm²
Length: 7.32 cm
III
Area: 3.834 cm²
Length: 7.35 cm
Panel C: Calcific Raphe
I
II
Area: 1.434 cm²
Length: 5.85 cm
III
Area: 2.771 cm²
Length: 5.97 cm
Panel D: Extensive calcification (Raphe & Leaflets)
I
II
Area: 1.846 cm²
Length: 7.89 cm
III
Area: 4.025 cm²
Length: 7.92 cm



Panel A
Panel B
Angle: 120.07°
9.38 mm
9.77 mm
Angle: 120.47°
Angle: 119.26°
9.48 mm
2.30 cm
1.77 cm
Angle: 112.42°
1.02 cm
1.02 cm
Angle: 123.46°
Angle: 119.59°
1.09 cm
2.73 cm
1.30 cm