

Transcatheter self-expanding valve replacement in pure native aortic regurgitation: Results from a multicenter registry study

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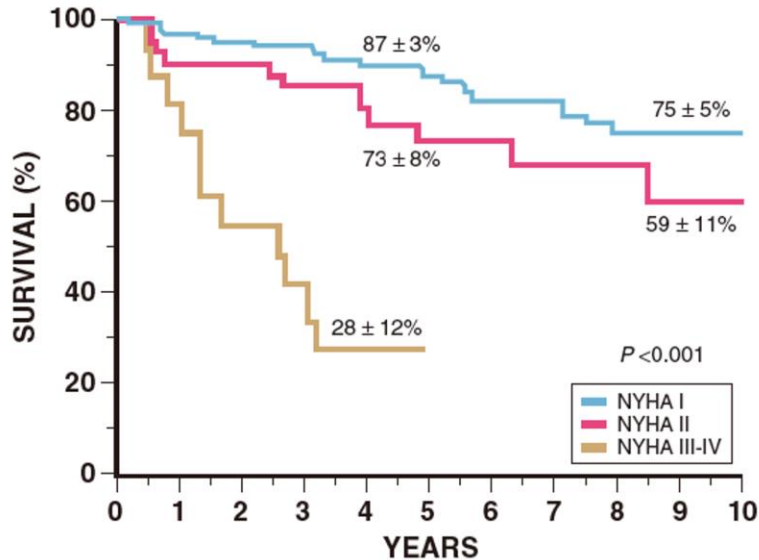
Nanjing Medical University

On behalf of SEASON-AR Trial Investigator

Disclosure of Relevant Financial Relationships

I, [Junjie Zhang] DO NOT have any relevant financial relationships to disclose.

Background (1)



Annual mortality rate is correlated with NYHA functional class in patients with chronic aortic regurgitation (AR)

- ✓ Among patients with severe native AR, only 21.8% with LVEF 30–50% and 2.7% with LVEF <30% were referred for surgical aortic valvular replacement (SAVR)
- ✓ Advanced age and comorbidities were often given as reasons not to offer SAVR
- ✓ The annual mortality of untreated patients with severe AR is 10–20%.

2021 ESC/EACTS guideline for VHD

Patients with AR with significant enlarged ascending aorta

- ❖ Severe AR + symptoms, or
- ❖ LVEF ≤50% or LVESD >50 mm or >25 mm/m² (BSA)

Surgery

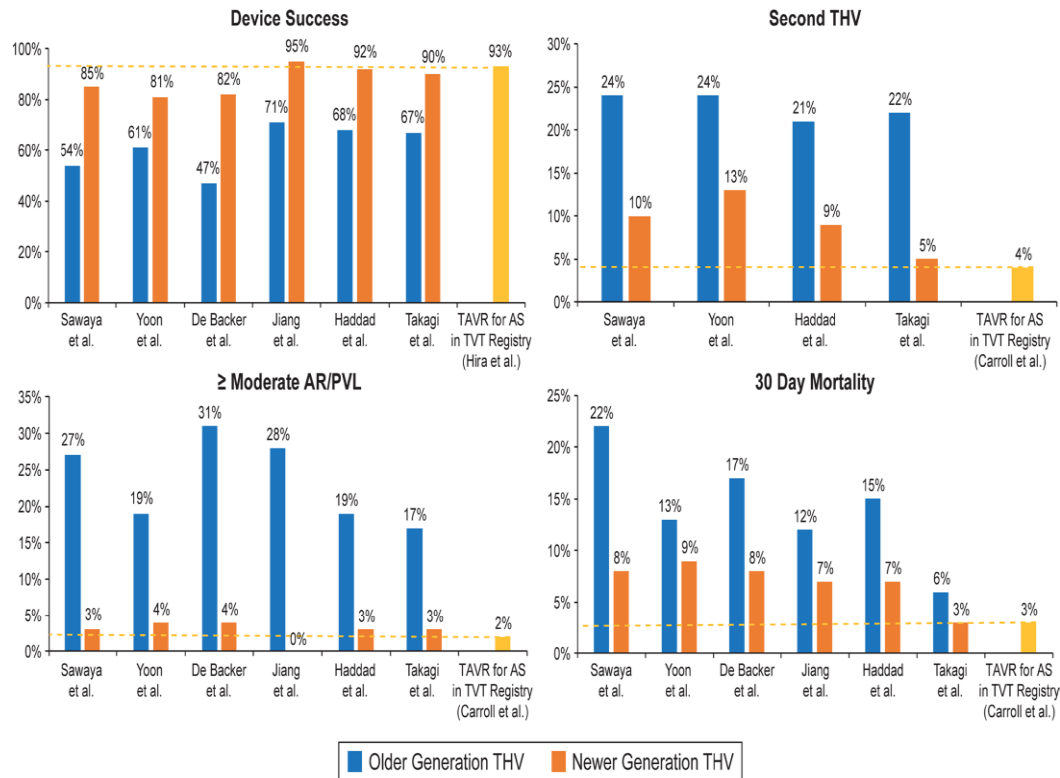
Challenges of TAVR for pure native AR

Anatomic

- Large aortic sinuses and annuli
- Concomitant aortic dilation
- Insufficient anchoring (less calcium)

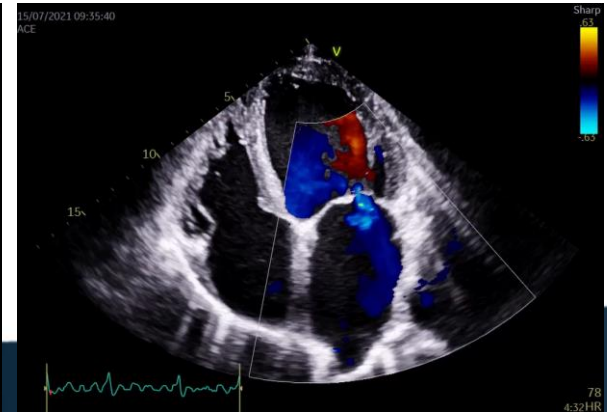
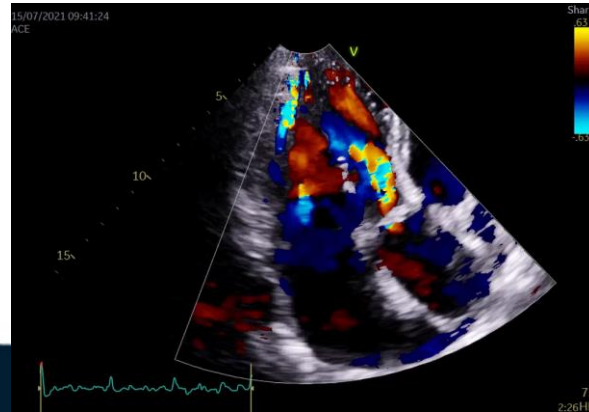
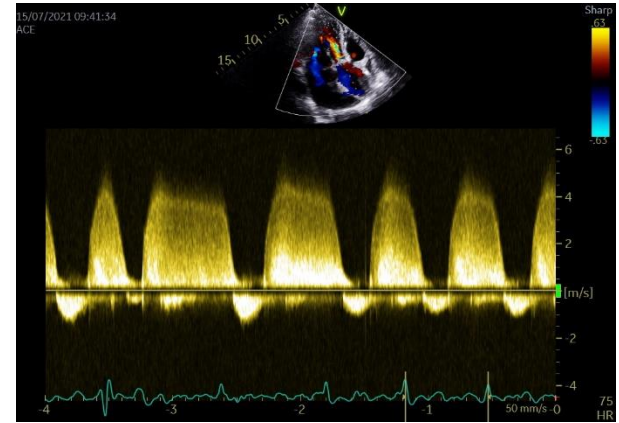
Procedural

- Lack of fluoroscopic visualization
- THV migration/embolization
- Residual aortic regurgitation
- Permanent pacemaker rates

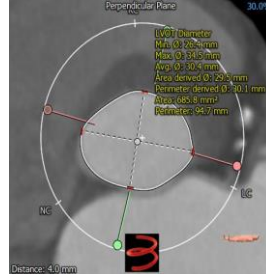
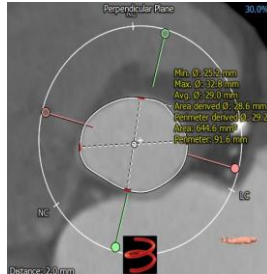


Case 1 TAVR for AR

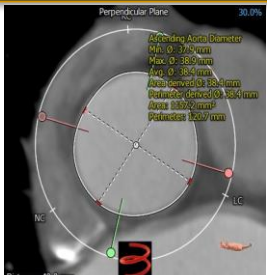
- 78ys, male, 178 cm, 55 kg, BMI 17.4kg/m²
- Exertional dyspnea for 2 years (Noninvasive Ventilator)
- Comorbidities: persistent AF, COPD, subtotal gastrectomy
- NT-pro BNP: 5366.26pg/ml, eGFR: 60.06 mL/min
- **STS score: 12.487% ; ECHO: LVEF:30%, LVEDD: 70mm**
- Clinical diagnosis: Severe AR



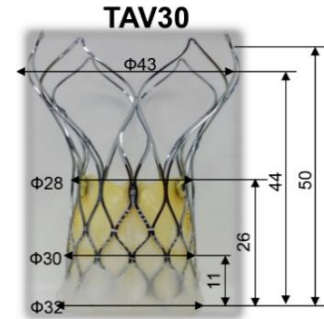
Baseline CT



Annulus P: 87.6 mm D: 27.4 mm	LVOT-2mm P: 91.6 mm D: 29.0 mm	LVOT-4mm P: 94.7 mm D: 30.4 mm
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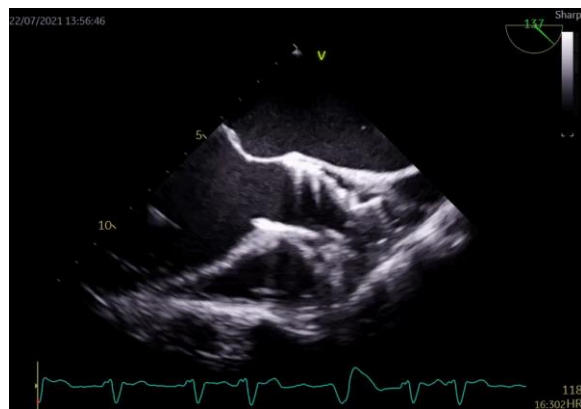
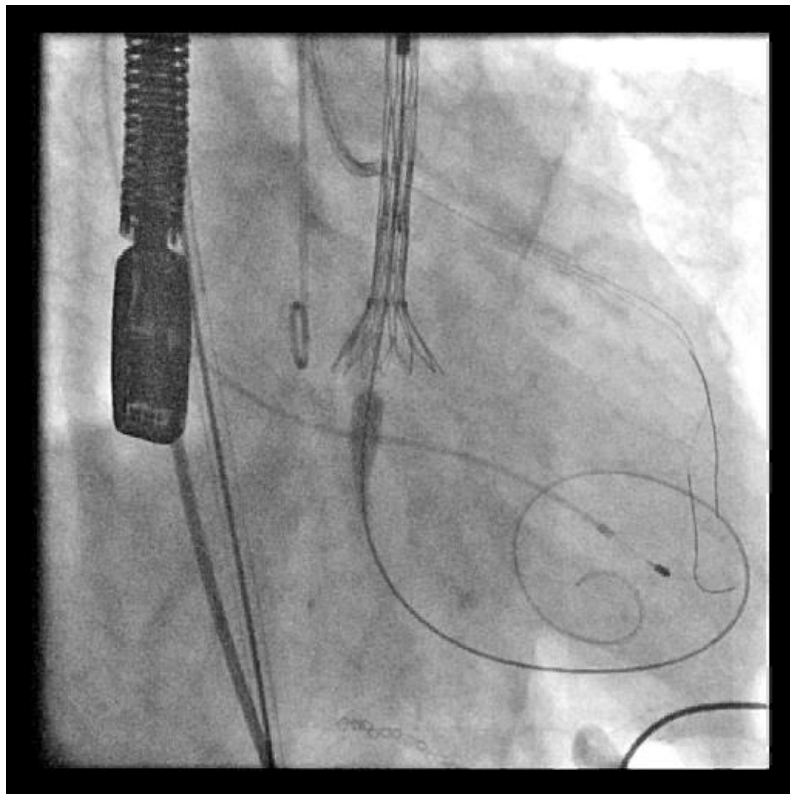
STJ Height: 22.8 mm D: 34.9 mm	AAO P: 120.7 mm D: 38.4 mm	SOV Maximum D: 38.6 mm Minimum D: 36.7 mm
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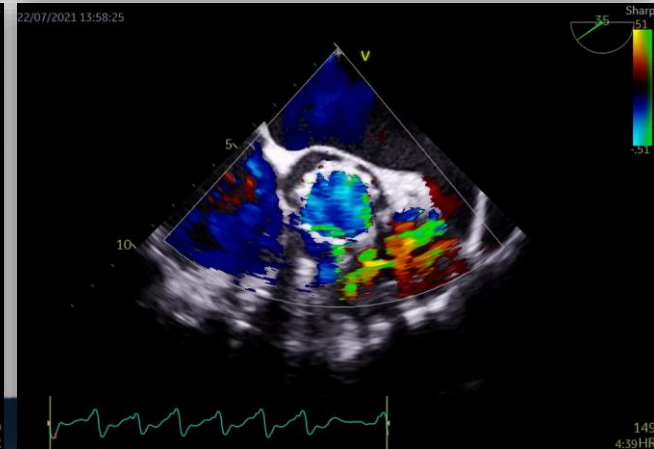
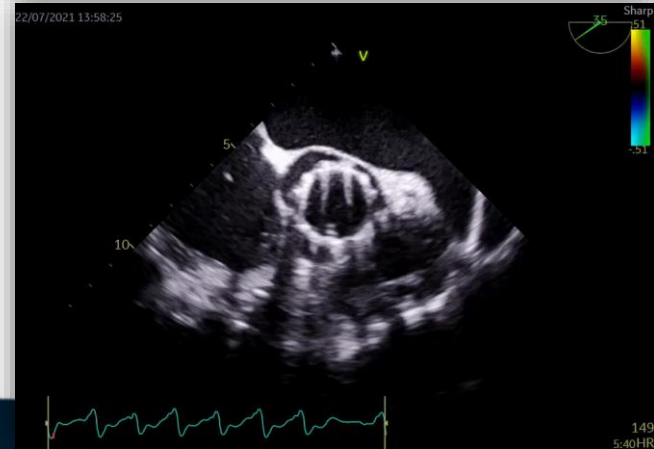
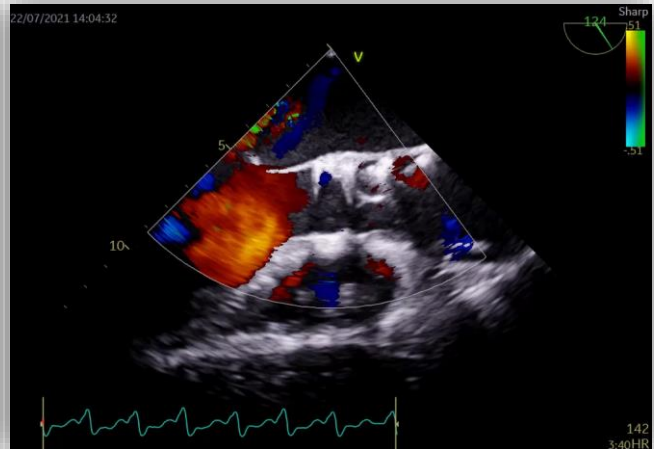
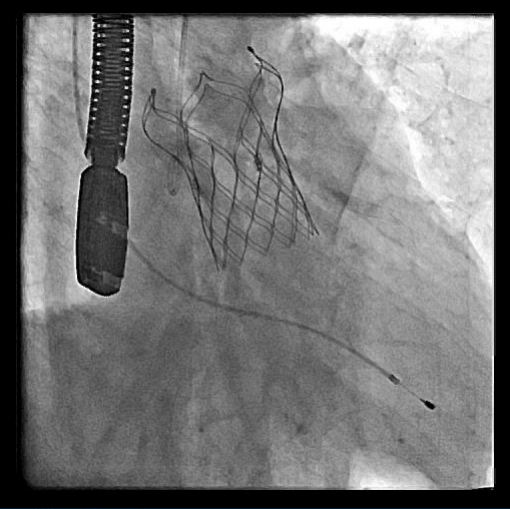
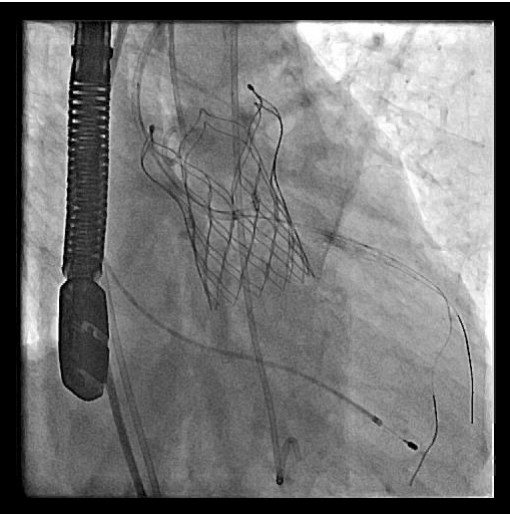
TAV30			
26	27	28	29
81.6	84.8	87.9	91.1
530.9	572.6	615.8	660.2

Upsize index :1.08

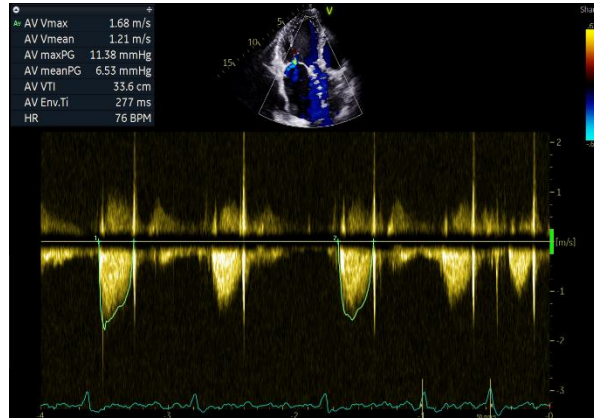
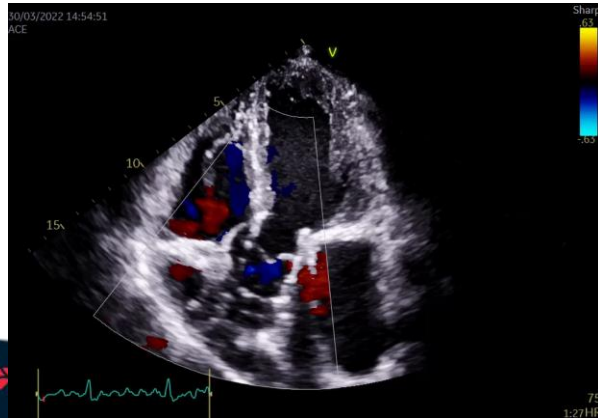
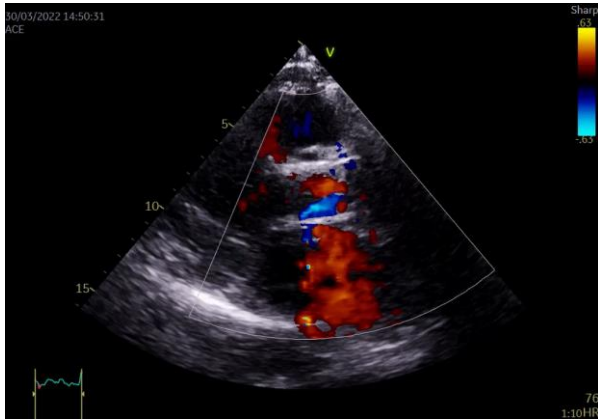
TEE-guided TAVR for AR (VitaFlow I 30)



Final results



FU at 6 months



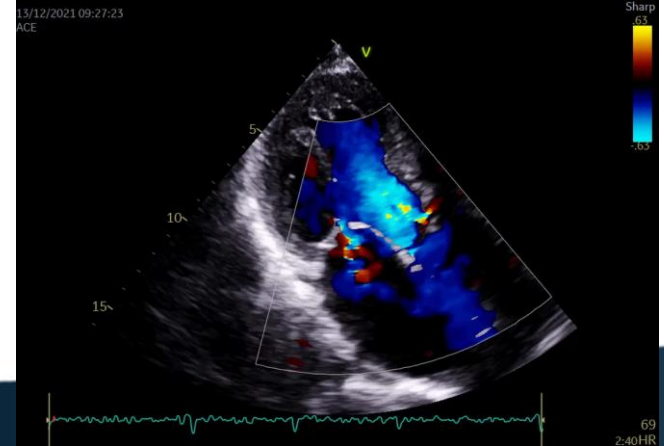
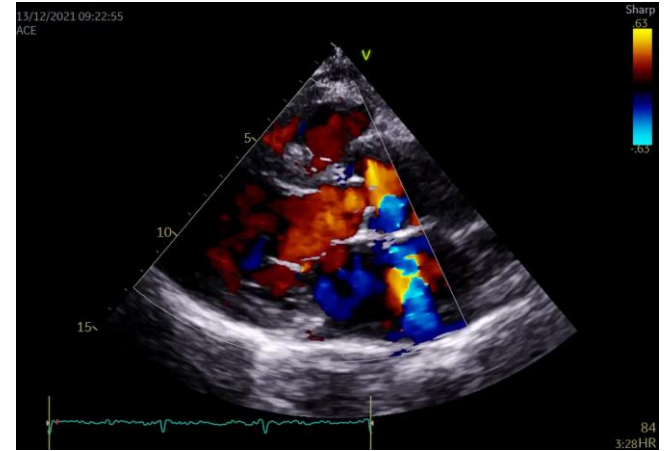
V max	1.7 m/s
Mean PG	6.5 mmHg
AVA	2.0 cm ²
LVEF	47%
LVEDd	58 mm



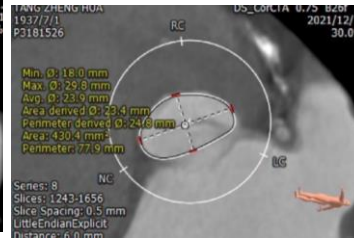
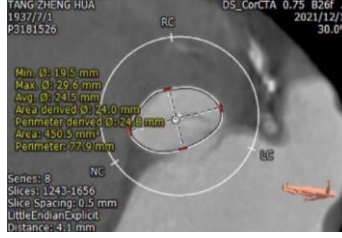
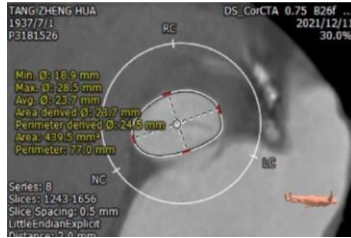
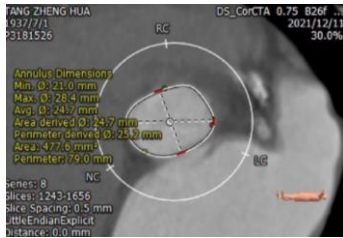
6WMD: 324 m

CASE 2-TAVR for AR

- 84ys, male, BMI: 19.6
- Exertional chest distress for 2 yrs, aggravated for one month
- Comorbidities: EH and atrial fibrillation for 10 yrs
- NYHA class III
- NT-pro BNP: 13466. pg/ml, eGFR: 48.2 mL/min/1.73m²
- ECG: atrial fibrillation
- STS score: 12.076%



Baseline CTA



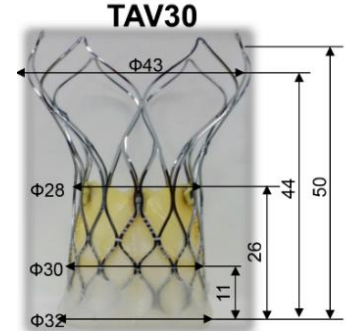
Annulus
P: 79.0 mm
D: 25.2 mm

LVOT-2 mm
P: 77.0 mm
D: 24.5 mm

LVOT-4 mm
P: 77.9 mm
D: 24.8 mm

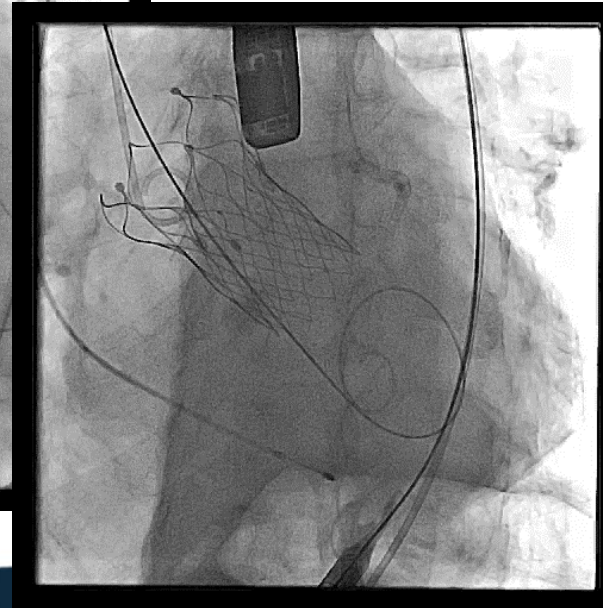
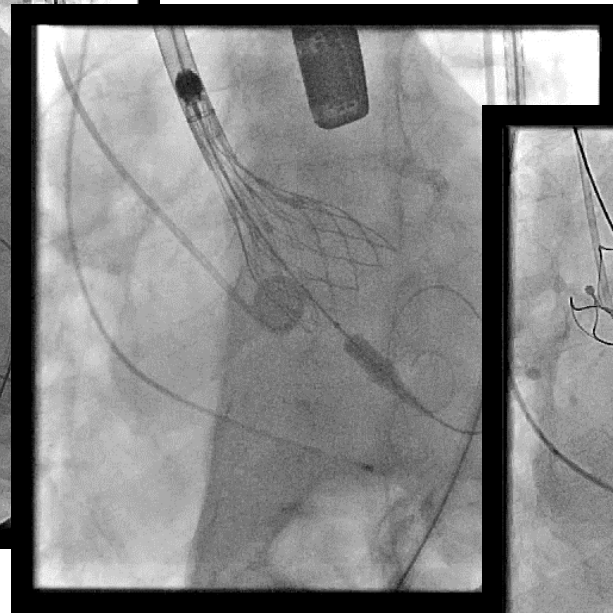
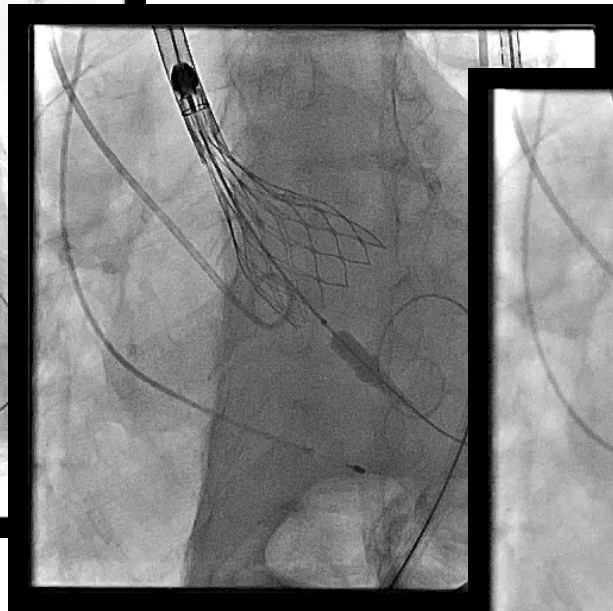
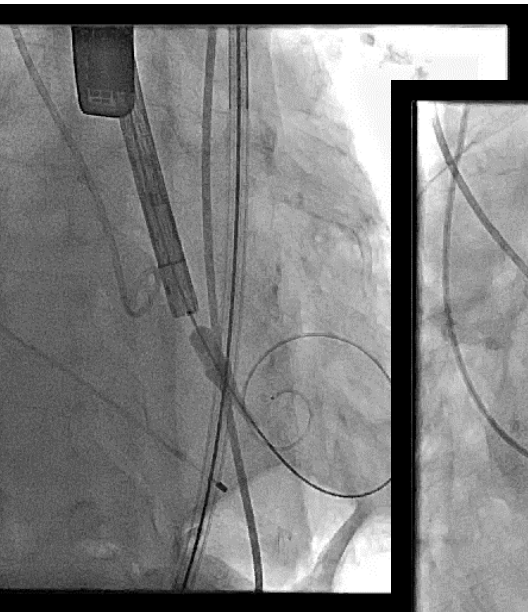
LVOT-6 mm
P: 77.9 mm
D: 24.8 mm

Upsize index :1.19



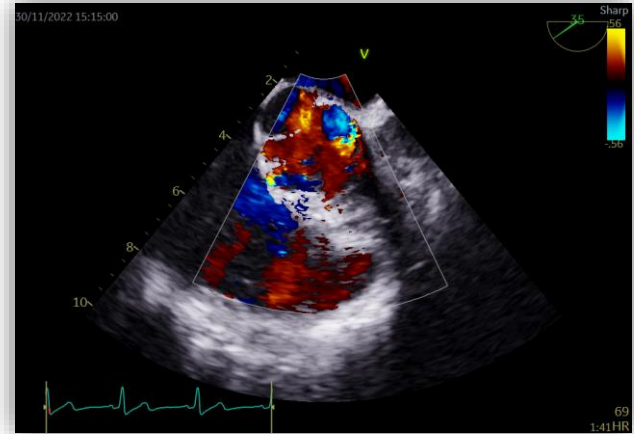
TAV30			
26	27	28	29
81.6	84.8	87.9	91.1
530.9	572.6	615.8	660.2

TEE-guided TAVR for AR (VitaFlow II 30)

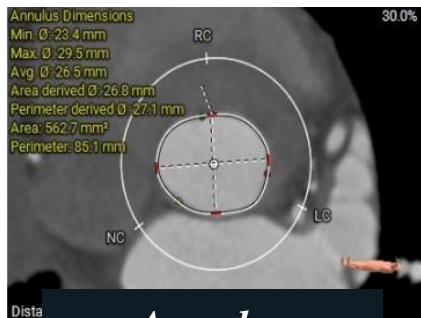


Case 3-TAVR for AR

- ◆ 79 yrs, male, BMI: 21.8
- ◆ Progressive shortness of breath over the past 2 yrs
- ◆ Comorbidities: EH and COPD for more than 20 yrs
- ◆ NYHA class IV
- ◆ NT-pro BNP: 6638.27/ml, eGFR: 61.95 mL/min/1.73m²
- ◆ ECG: normal
- ◆ STS score: 9.663%



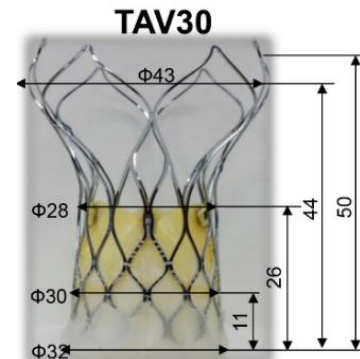
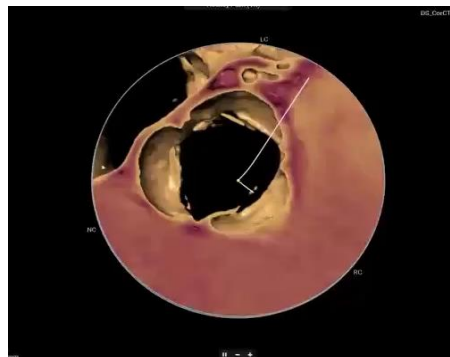
Baseline CTA



Annulus
Avg. Φ : 26.5 mm



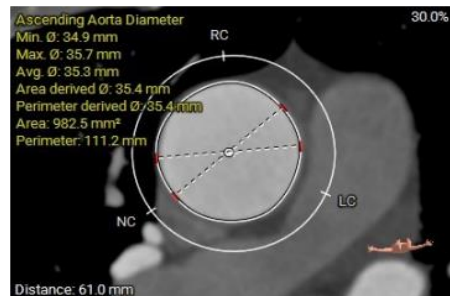
LVOT-2 mm
Avg. Φ : 27.1 mm



LVOT-4 mm
Avg. Φ : 28.1 mm



LVOT-6 mm
Avg. Φ : 30.7 mm

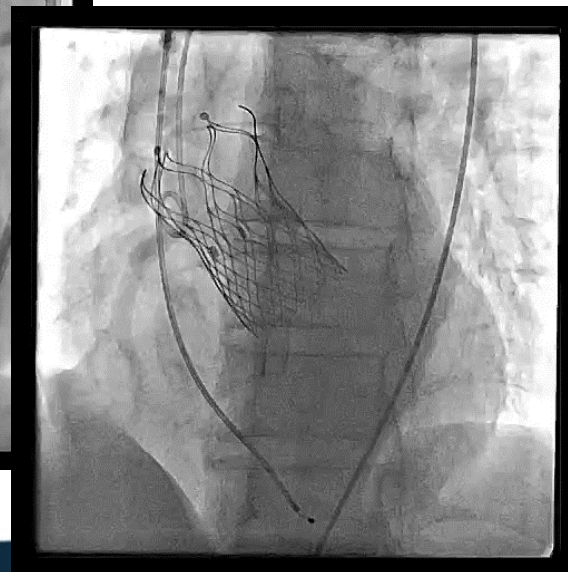
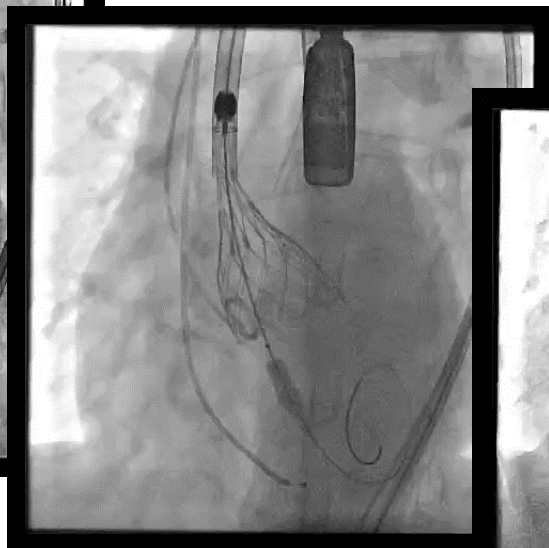
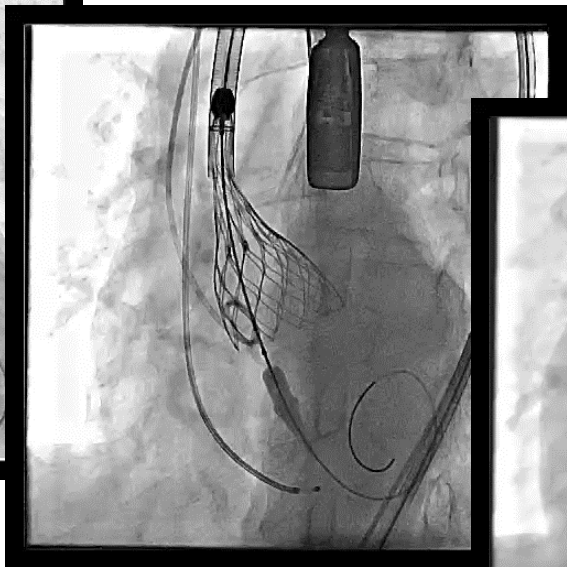
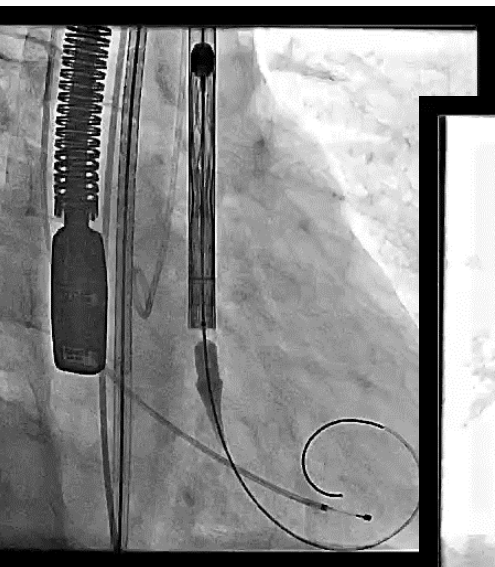


AAO
Avg. Φ : 35.3 mm

TAV30				
→				
26	27	28	29	
81.6	84.8	87.9	91.1	
530.9	572.6	615.8	660.2	

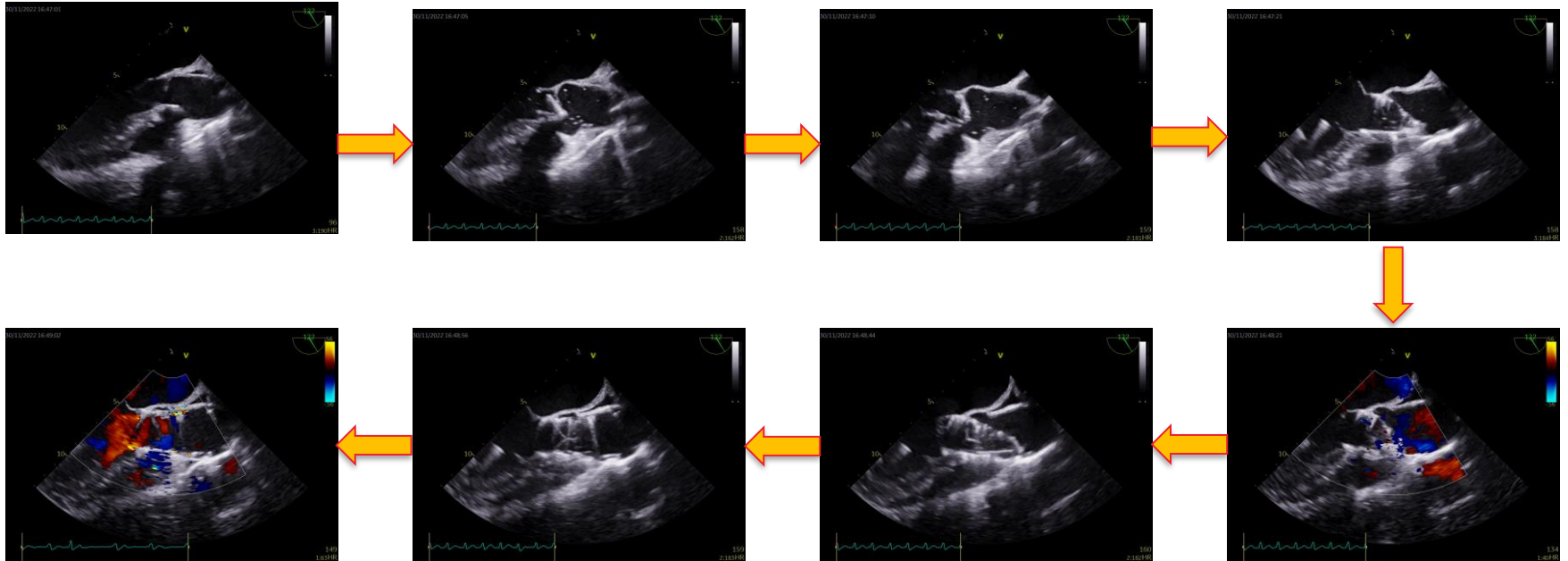
Upsize index :1.11

TEE-guided TAVR for AR (VitaFlow II 30)



Oversize index :1.11

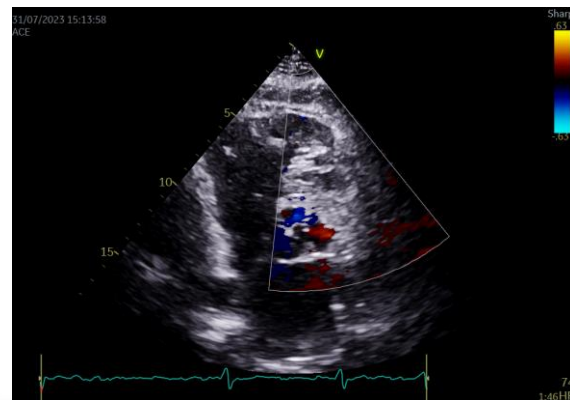
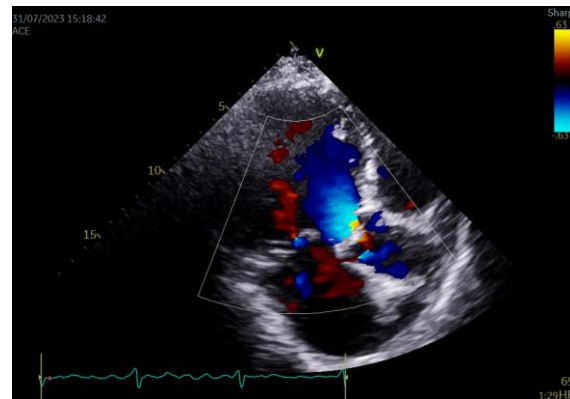
Intraoperative TEE



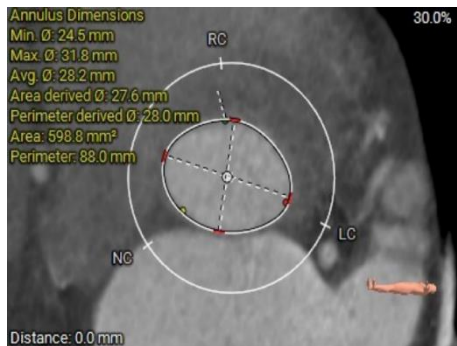
Case 4-TAVR for AR

84 yrs male, BMI: 23.88 kg/m²

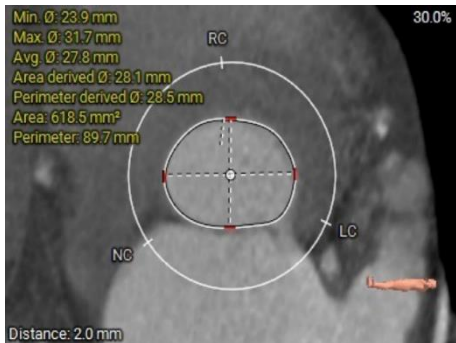
- **Repeated dysnpea for 2 years**
- **BNP: 481.83 pg/ml,**
- **STS score: 4.84%**
- **Diagnose: VHD, AR, Af, NYHA III**



Baseline CTA



Annulus
 Avg. Φ : 28mm



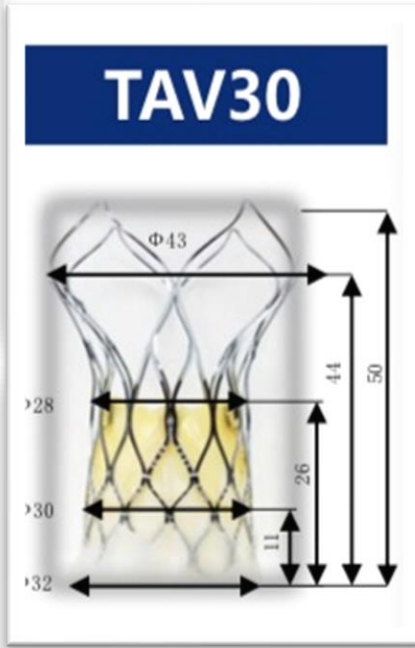
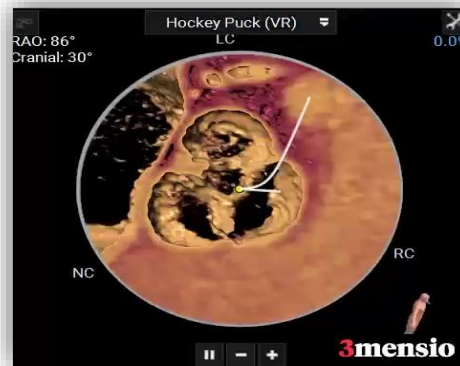
LVOT-2 mm
 Avg. Φ : 28.5mm



LVOT-4 mm
 Avg. Φ : 31.4 mm

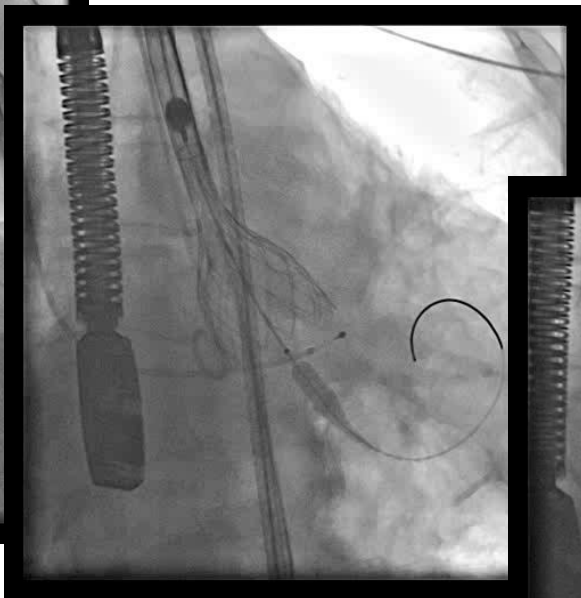
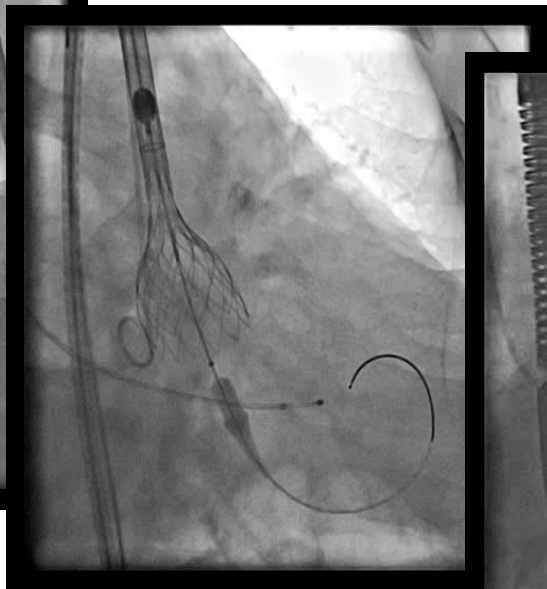
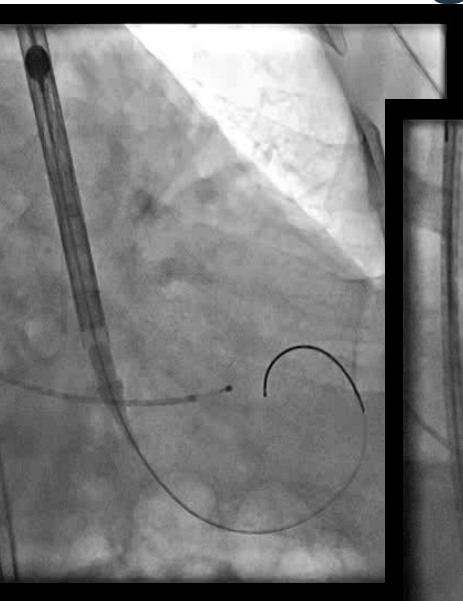


AAO
 Avg. Φ : 36 mm



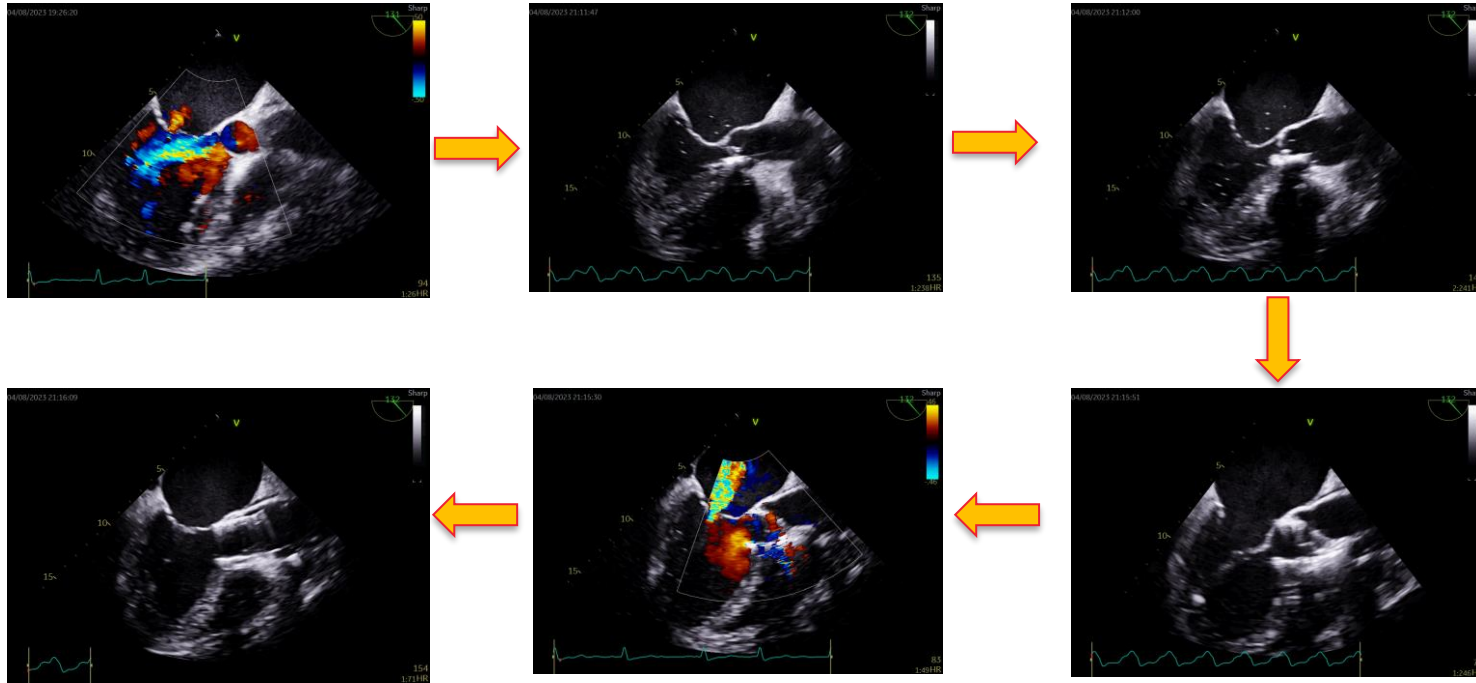
Upsize index :1.07

TEE-guided TAVR for AR (VitaFlow II 30)



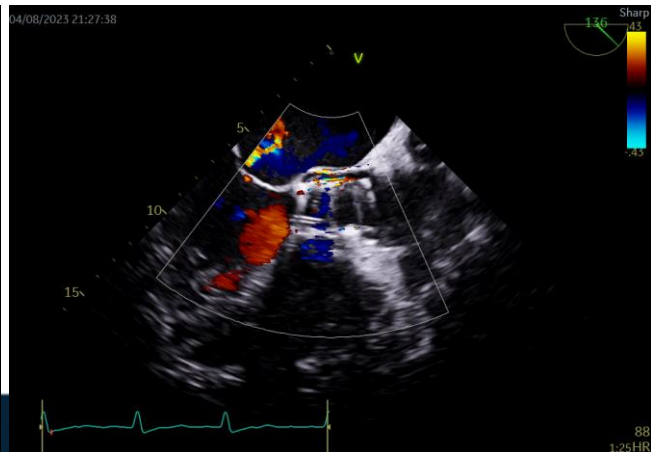
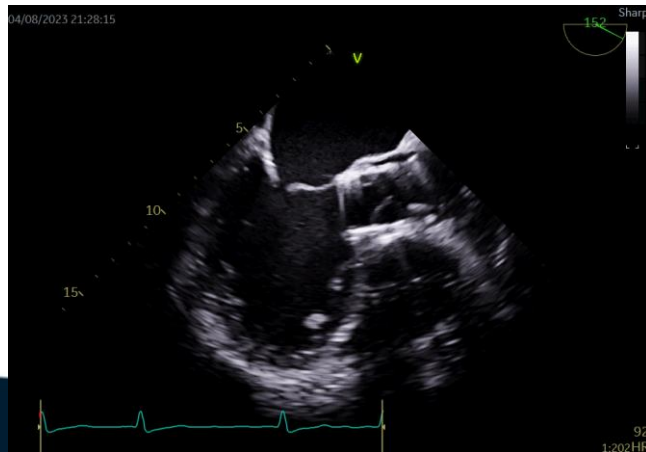
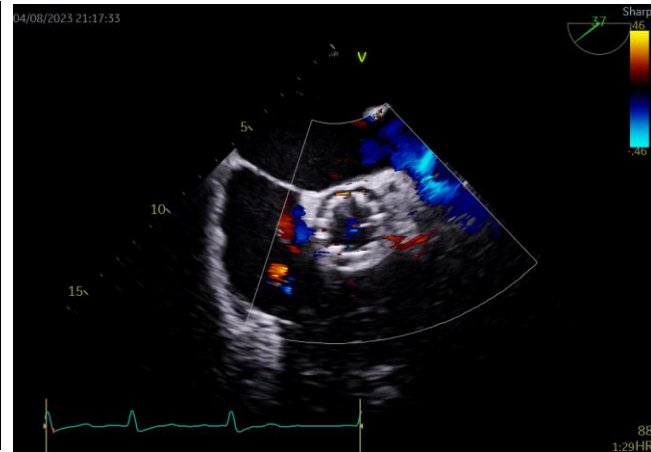
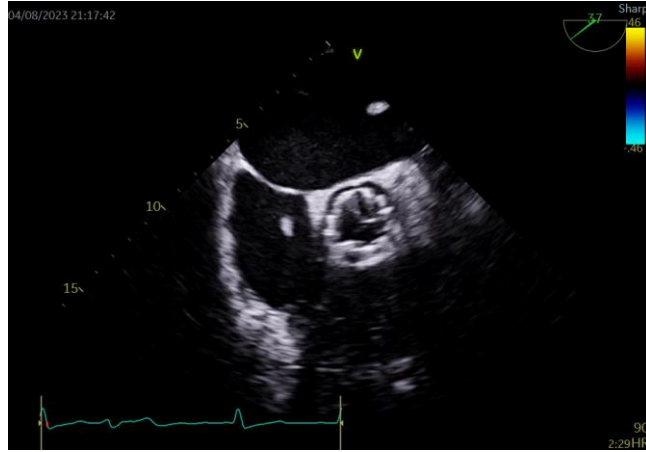
Upsize index :1.07

Intraoperative TEE

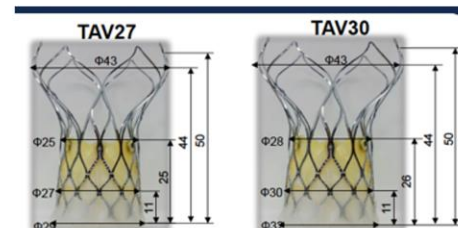
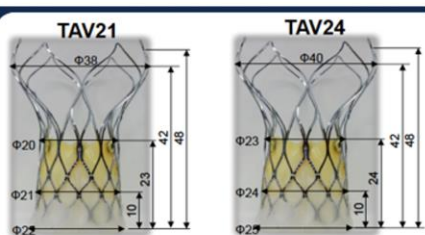


Upsize index :1.07

Final Result of TEE



Study flowchart



SEASON-AR trial (severe AR)

Registry arm

Patients with pure AR patients who underwent TAVR in 5 centers from September 2019 to February 2022

6-month clinical follow-up (n=79)

Randomization arm

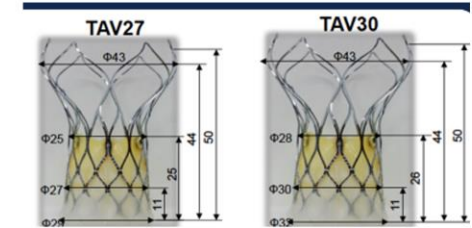
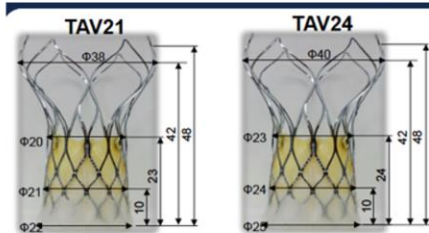
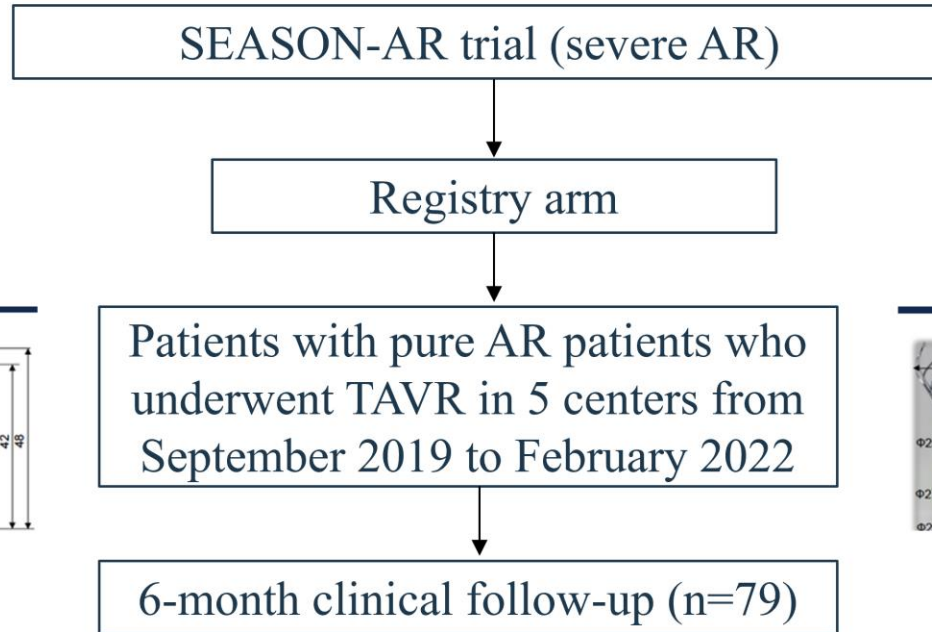
TAVR (n=105)

Medication (n=105)

On-going

12-month clinical follow-up

Study flowchart



Aims of SEASON-AR trial

We aimed to determine:

- Device success rate
- Independent factors of device failure
- 30-day mortality
- 6~12 months clinical outcomes

Baseline characteristics

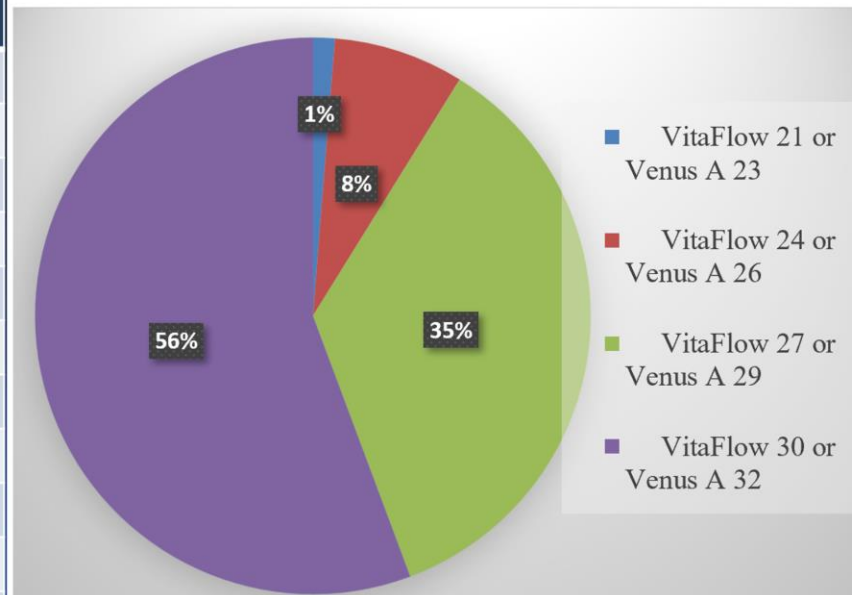
	AR patients n = 79
Age, yrs	72 ± 7.6
Hypertension, n (%)	55 (69.6)
Diabetes, n (%)	11 (13.9)
Previous MI, n (%)	8 (10.1)
STS risk score, score	6.03 ± 3.15
LVEF, %	52.42 ± 11.17

CT measurements prior-to procedure

	Total patients (n=79)
Aortic annulus perimeter, mm	78.58 ± 6.52
Perimeter of LVOT-4, mm	82.16 ± 10.11
Left coronary height, mm	13.74 ± 3.19
Right coronary height, mm	16.20 ± 3.49
Sinotubular junction diameter, mm	33.89 ± 5.52
Sinotubular junction height, mm	24.22 ± 4.84
Ascending aorta diameter, mm	40.80 ± 6.75
Aortic valve calcification (850HU), mm ³	6.35 ± 17.28
Calcification 0, mm ³	59 (75.6)

Procedural characteristics

	Total patients (n=79)
General anesthesia	79 (100)
TEE guidance	79 (100)
Transfemoral approach	79 (100)
Prosthesis Type	
VitaFlow (Early-generation)	51 (64.6)
VitaFlow (New-generation)	11 (13.9)
Venus A (Early-generation)	14 (17.7)
Venus A (New-generation)	3 (3.8)
Oversizing index, %	15.3 ± 6.5
TAVR+PCI	9 (11.4)
Balloon pre-dilation	10 (12.7)
Balloon post-dilation	1 (1.3)



Procedural complications

	Total patients (n=79)	TVT registry* (n=230)
All-cause mortality	1 (1.3)	28 (12.2)
Cardiovascular mortality	1 (1.3)	-
Second valve used	15 (19.0)	42 (18.3)
Early-generation valve	14/65 (21.5)	27/81 (33.3)
New-generation valve	1/14 (7.1)	15/149 (10.1)
Moderate-severe PVL	2 (2.5)	21/199 (10.5)
Ischemic stroke	1 (1.3)	5 (2.2)
Valve migration	4 (5.1)	13 (5.7)
Emergency conversion to cardiac surgery	2 (2.5)	-
Vascular complication	4 (5.1)	8 (3.5)
Minor vascular complication	4 (5.1)	5 (2.2)
New permanent pacemaker implantation	22 (27.8)	43 (18.7)
For type II or III AVB	17 (21.5)	-
For LBBB + type I AVB	5 (6.3)	-

*Anwaruddin S, et al. Am J Cardiol. 2019;124:781-788.



1-month clinical outcome

	Total patients (n=79)	TVT registry* (n=230)	Difference (95% CI)
All-cause mortality	1 (1.3)	28 (12.2)	10.9 (0.03-0.16)
Second valve used	15 (18.9)	42 (18.3)	----
Moderate-severe PVL	2 (2.5)	21/199 (10.5)	8.0 (-0.001-0.14)
Ischemic stroke	1 (1.3)	5 (2.2)	----
Valve migration	4 (5.1)	13 (5.7)	----
Urgent cardiac surgery	2 (2.5)	-	----
Vascular complication	4 (5.1)	8 (3.5)	----
New permanent pacemaker implantation	22 (27.9)	43 (18.7)	9.2 (-0.02-0.21)
For type II or III AVB	17 (21.5)	-	
For LBBB + type I AVB	5 (6.3)	-	

6-month clinical outcome

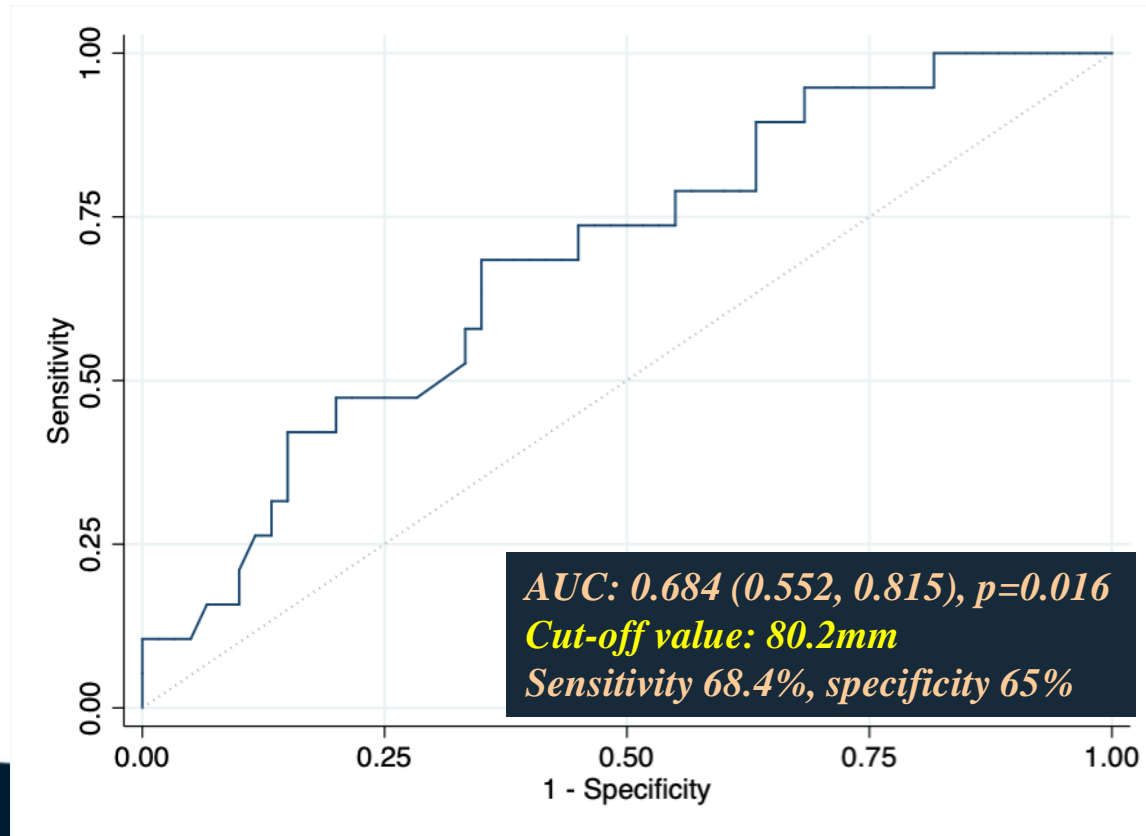
	Total patients (n=79)
MACE	29 (36.7)
All-cause mortality	4 (5.1)
Ischemic stroke	1 (1.3)
Heart failure rehospitalization	3 (3.8)
New permanent pacemaker implantation	25 (31.6)
For type II or III AVB	19 (24.1)
For LBBB + type I AVB	6 (7.6)

Predictors of 1-month device success

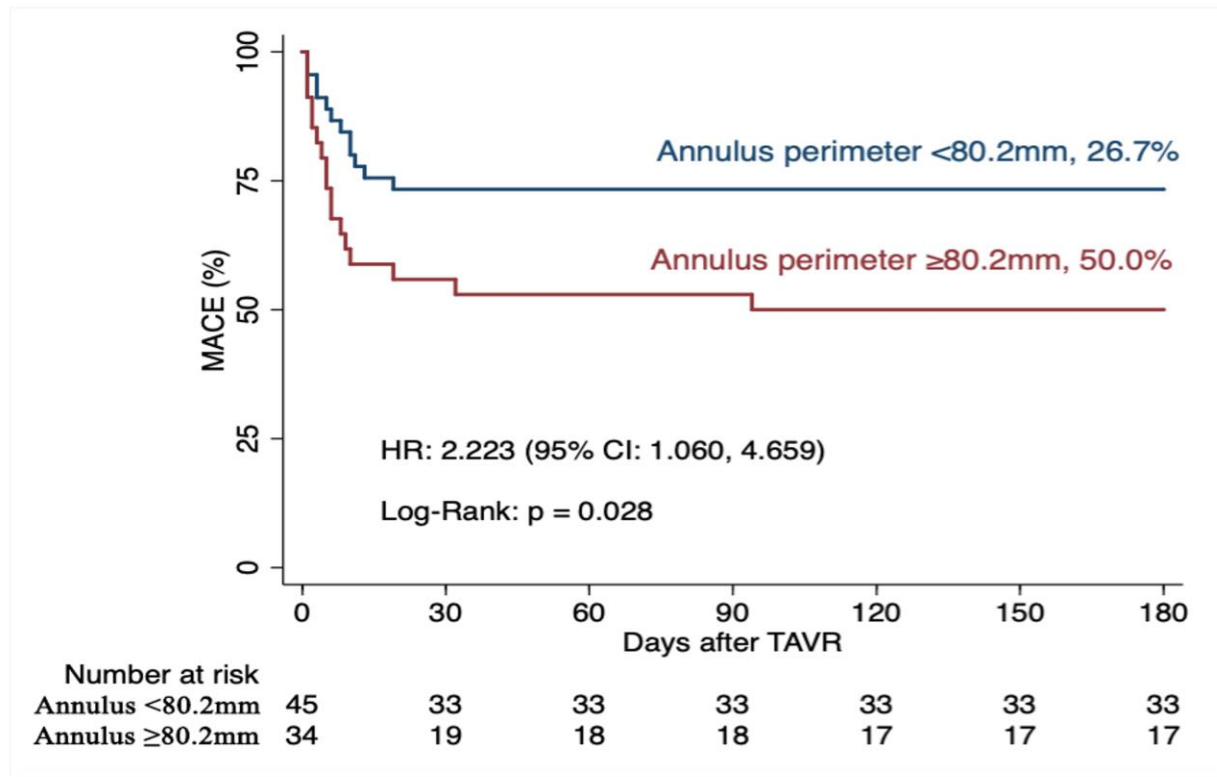
Variables	OR (95% CI)	p value
Age	1.032 (0.936, 1.138)	0.525
Female	0.873 (0.135, 5.629)	0.887
Hypertension	2.253 (0.495, 10.248)	0.293
Diabetes	0.376 (0.055, 2.579)	0.320
Chronic obstructive pulmonary disease	0.266 (0.029, 2.426)	0.240
STS score	0.760 (0.584, 0.989)	0.041
LVEF	0.998 (0.936, 1.066)	0.963
Annulus perimeter	0.888 (0.796, 0.992)	0.035

ROC Curve

Annulus perimeter predicting device success



Kaplan-Meier analysis at 6-month FU



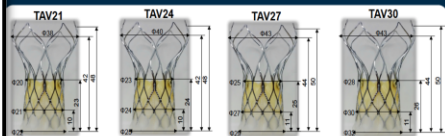
TTE before TAVR and during follow-up

	Baseline TTE (n=42)	Follow-up TTE (n=42)	p value
LVEDD, mm	62.0 ± 5.7	54.4 ± 5.9	<0.001
LVESD, mm	44.6 ± 7.5	37.1 ± 6.7	<0.001
LVEDV index, mL/m²	120.3 ± 25.5	89.9 ± 26.1	<0.001
LVESV index, mL/m²	58.0 ± 23.6	38.5 ± 19.8	<0.001
LVEF, %	52.2 ± 11.7	58.4 ± 9.3	<0.001
Cardiac output, L/min	4.1 ± 0.9	4.5 ± 0.9	<0.001
Cardiac index, L/(min·m²)	2.5 ± 0.6	2.8 ± 0.5	<0.001
Left atrial volume index, mL/m²	35.9 ± 10.9	33.4 ± 11.3	0.038
Left ventricular mass index, g/m²	161.3 ± 36.0	130.0 ± 26.4	<0.001

- Core-lab reported data.
- 13 patients with permanent pacemaker implantation.
- Median FU: 188 days (IR: 117 to 271 days).

SEASON-AR Trial

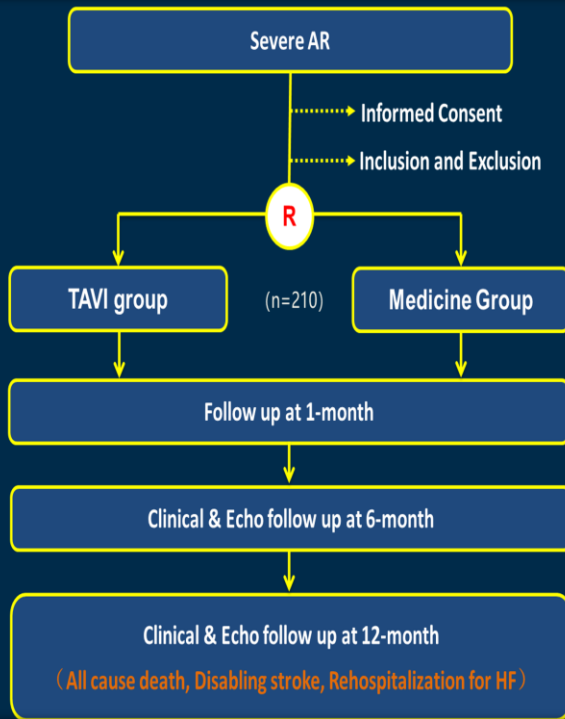
Self-expandable valve in the treatment of severe native aortic regurgitation: a prospective, multicenter, randomized study (SEASON-AR trial)



Leading Center: Nanjing First Hospital

Principle Investigator: Jun-Jie Zhang, Shao-Liang Chen

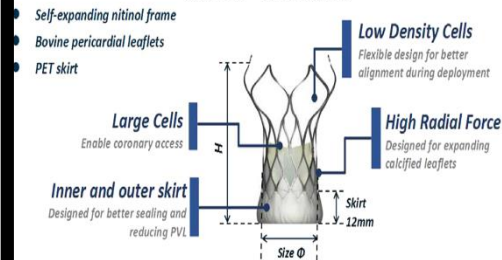
ClinicalTrials.gov ID: **NCT04864145**



Inclusion criteria

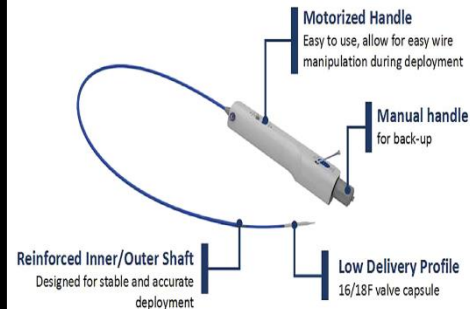
- Symptomatic AR;
- TTE confirmed severe AR, mean gradient <20mmHg;
- No symptom+ LVEF ≤ 55%
 - Or LVEDD > 65mm
 - Or LVESD > 50mm;
- MDCT or 3D-TEE confirmed annulus perimeter ≤ 85 mm;
- MDCT or 3D-TEE confirmed perimeter ratio of LVOT-4mm/Annulus varies from 0.95 to 1.05
- STS score ≥ 8; Frailty; Strongly reject AVP surgery; Heart team confirmed extreme risk of surgery

VitaFlow™ Aortic Valve



Size Ø	21mm	24mm	27mm	30mm
Aortic Annulus Diameter	17-20mm	20-23mm	23-26mm	26-29mm
Height H	50mm	50mm	53mm	53mm

VitaFlow™ Delivery System



Summary

- TF-TAVR with self-expanding valve could be considered an option in pure severe AR patients not suitable for surgery, with acceptable device success, increased new permanent pacemaker implantation rate, and improved left ventricular function after TAVR.
- Device success and clinical efficacy could be improved significantly in AR patients with appropriate annulus perimeter.
- SEASON-AR trial is ongoing to demonstrate the benefit of TAVR for pure AR with high risk for surgery.
- Dedicated TAVR devices with trans-femoral approach need to be developed for pure AR.