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Transcatheter or Surgical Aortic Valve Replacement in Patients with Severe Aortic Stenosis and Small Aortic Annulus: A Randomized Clinical Trial

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On behalf of the VIVA trial investigators

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Background

- Current guidelines recommend both SAVR and TAVR for treating older patients with aortic stenosis. However, aortic annular size, prosthetic valve hemodynamics, and gender factors are not taken into consideration in current guideline recommendations.
- Data from observational studies and sub-studies from randomized trials suggest superior prosthetic valve performance following TAVR (vs. SAVR) in patients with small aortic annulus.
- Several studies have reported improved outcomes associated with TAVR in women patients, which constitute a population with a high prevalence of small aortic annulus. However, women have often been largely under-represented in heart valve trials.

Objective

To compare the hemodynamic and clinical outcomes between transcatheter aortic valve replacement (TAVR) and surgical aortic valve replacement (SAVR) in patients with severe aortic stenosis and small aortic annulus.

Methods

- Investigator initiated multicentre trial, including 15 centres (Canada, Europe, Brazil).
- Prospective randomized controlled trial (NCT03383445).
- Patients with severe aortic stenosis and a small aortic annulus were randomized (1:1) to TAVR or SAVR.
- Patients were followed at 30, 60 days, 1 year, and yearly thereafter up to 5 years.
- Echocardiography data (baseline, 60 days) were analyzed in a central Echo Core Lab (Quebec Heart & Lung Institute).

Methods

Inclusion criteria

- Patients ≥65 years old with severe aortic stenosis accepted for aortic valve replacement and eligible for TAVR or SAVR according to Heart Team evaluation.
- Small aortic annulus (mean diameter: <23 mm, minimal diameter: ≤21.5 mm) as evaluated by contrast computed tomography.
- No concomitant mitral or tricuspid valve disease; no aortic root dilation >45 mm; no prior aortic valve surgery; no coronary artery disease with SYNTAX score >32.

Primary outcome

- Impaired valve hemodynamics defined as the occurrence of severe prosthesis-patient mismatch (PPM) and/or moderate-severe aortic regurgitation (AR) as evaluated by Doppler-echocardiography at 60 days (VARC-2 definitions).

Secondary outcomes

- Clinical endpoints (death, stroke, major or life-threatening bleeding, new-onset atrial fibrillation, permanent pacemaker implantation, cardiac rehospitalization) at 30 days and at follow-up (VARC-2 definitions).

Methods

Procedures

TAVR

- Transfemoral as default access.
- SAPIEN 3/Ultra, Evolut R/PRO/PRO+/FX, ACURATE neo/neo2 valves.
- Valve sizing according to manufacturer recommendations, based on CT measurements.

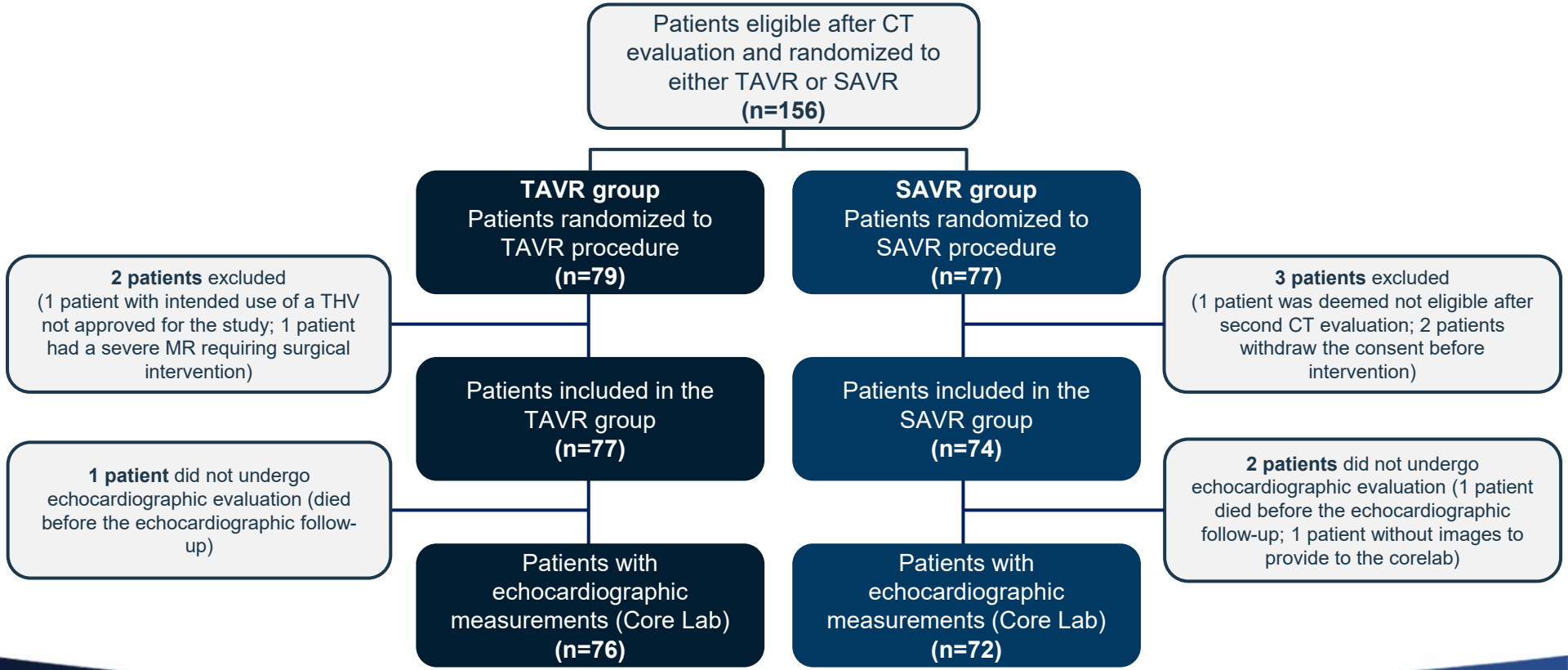
SAVR

- Any valve type approved for clinical use.
- Aortic root enlargement left to the criteria of the surgeon responsible for the intervention.

Sample size

- Initial sample size estimated at 300 patients (superiority of TAVR).
- Slow enrolment: COVID-19 pandemic + results of the PARTNER 3 and Evolut Low Risk trials; early cessation of the trial, after the inclusion of 156 patients (52% of the estimated study population).

Study Population Flowchart



Baseline Characteristics

	TAVR (n=77)	SAVR (n=74)	*P* value
Clinical Characteristics			
Age, years	75.9±5.3	75.1±4.9	0.34
Women	73 (94.8%)	67 (90.5%)	0.31
BSA, m^2	1.69±0.18	1.73±0.19	0.20
STS, %	2.55 (1.79-3.27)	2.43 (1.67-3.31)	0.85
Diabetes	23 (29.9%)	22 (29.7%)	0.99
Hypertension	62 (80.5%)	61 (82.4%)	0.76
Renal insufficiency	25 (32.5%)	26 (35.1%)	0.73
Aortic annulus diameter (CT), mm	21.2 (20.5-22.0)	21.0 (20.4-22.0)	0.66
Minimal aortic annulus diameter (CT), mm	19.0 (17.7-19.9)	18.5 (17.3-19.6)	0.22
Aortic annulus area (CT), mm^2	348±42	343±39	0.46
Aortic annulus perimeter (CT), mm	67.3±5.0	66.3±6.3	0.30
Echocardiographic data			
Left ventricular ejection fraction, %	62±7	62±8	0.66
Mean aortic gradient, mm Hg	47±17	49±17	0.54
Maximal aortic gradient, mm Hg	79±24	80±24	0.82
Aortic valve area, cm^2	0.67±0.18	0.74±0.36	0.19

Procedural Characteristics

	TAVR (n=77)	SAVR (n=74)	*P* value
Approach			
Transfemoral	69/76* (90.8%)	-	-
Transcarotid/Transaortic	7/76* (9.2%)	-	-
Valve type			
Balloon-expandable	31/76* (40.8%)	-	-
Self-expandable	45/76* (59.2%)	-	-
Stented (surgical)	-	56/71** (78.9%)	-
Sutureless (surgical)	-	15/71** (21.1%)	-
Aortic root enlargement	-	5/71** (7.0%)	-
PCI (preprocedure or at the time of TAVR) or **CABG** (at the time of SAVR)	10/77 (13.0%)	8/74 (10.8%)	0.70
Successful valve implantation	77 (100%)	73 (100%)	1.00
Need for a second valve	1 (1.3%)	-	-
Cardiac tamponade	1 (1.3%)	4 (5.4%)	0.20

*1 patient in the TAVR group finally underwent SAVR
**3 patients in the SAVR group finally did not receive a surgical valve (2 patients underwent TAVR and 1 patient had a commissurotomy)

Procedural Characteristics (Valve Types)

	TAVR	SAVR
SAPIEN 3/ Ultra	29/2	-
CoreValve Evolut R/ PRO/ PRO +/ FX	17/16/1/4	-
ACURATE neo/ neo2	4/3	-
Stented		
Avalus	-	1
Braile Biomedica	-	14
PERIMOUNT Magna Ease	-	18
INSPIRIS RESILIA	-	17
Trifecta	-	4
Mitroflow		1
Sutureless		
Perceval	-	15
INTUITY Elite	-	1

30-Day Outcomes

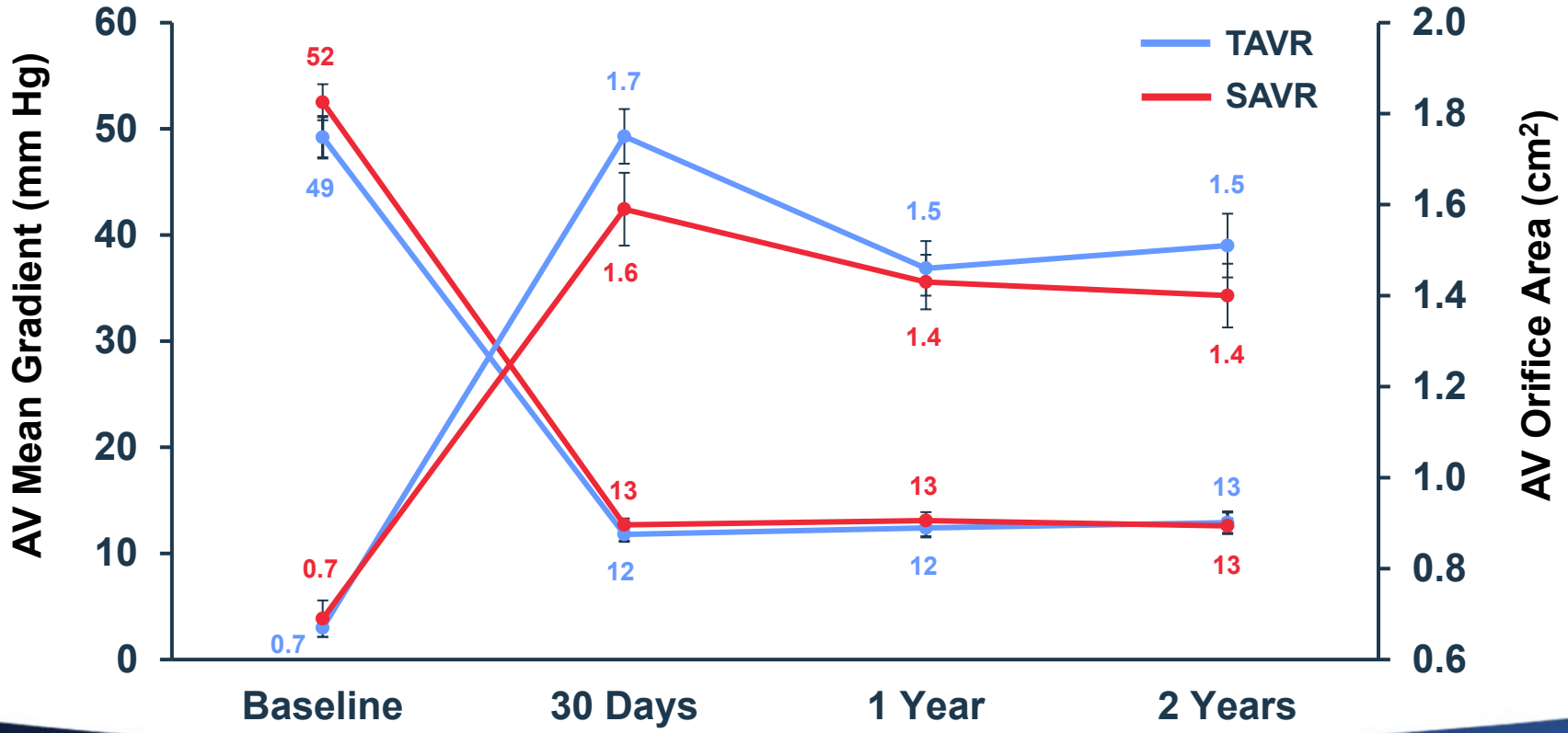
	TAVR (n= 77)	SAVR (n= 74)	TAVR vs SAVR (95%CI)	*P* Value
30-day outcomes				
Death	1 (1.3%)	1 (1.4%)	0.05 (-6.28 to 5.88)	1.00
Stroke	0 (0%)	2 (2.7%)	-2.70 (-9.42 to 2.27)	0.24
Disabling stroke	0 (0%)	2 (2.7%)	-2.70 (-9.42 to 2.27)	0.24
Death or stroke	1 (1.3%)	3 (4.1%)	-2.76 (-10.35 to 3.53)	0.36
Major/life-threatening bleeding	7 (9.1%)	16 (21.6%)	-12.53 (-24.97 to -0.85)	0.03
Myocardial infarction	2 (2.6%)	3 (4.1%)	-1.46 (-9.41 to 5.52)	0.68
New-onset atrial fibrillation	5 (6.5%)	20 (27.0 %)	-20.48 (-32.80 to -7.27)	<0.01
New-onset left bundle branch block	9 (11.7%)	3 (4.1%)	7.63 (-1.49 to 17.44)	0.13
New permanent pacemaker	9 (11.7%)	4 (5.4%)	6.28 (-3.10 to 16.28)	0.25
Aortic valve reintervention	2 (2.6%)	0 (0%)	2.60 (-2.78 to 9.39)	0.50
Coronary obstruction	0 (0%)	1 (1.4%)	-1.35 (-7.40 to 3.58)	0.49
Annulus rupture	1 (1.3%)	-	-	-

Valve Performance at 60 Days

	TAVR n=76	SAVR N=72	Difference TAVR-SAVR (95%CI)	*P* value
LVEF, %	61±6	61±8	0.30 (-2.27 to 2.87)	0.82
Mean aortic gradient, mmHg	11±5	11±5	0.31 (-1.29 to 1.91)	0.70
Mean gradient >20 mmHg	4 (5.3%)	7 (9.7%)	-4.46 (-13.85 to 3.93)	0.30
Maximal aortic gradient, mmHg	22±9	21±9	0.66 (-2.24 to 3.56)	0.65
Effective orifice area, cm^2	1.63±0.40	1.65±0.45	-0.02 (-0.16 to 0.12)	0.79
Effective orifice area indexed, cm^2/m^2	0.99±0.28	0.98±0.27	0.01 (-0.08 to 0.11)	0.76
Velocity ratio	0.50±0.11	0.50±0.11	0.00 (-0.03 to 0.04)	0.81
Severe PPM or moderate-severe AR (*Primary Outcome*)	4/72 (5.6%)	7/68 (10.3%)	-4.74 (-13.69 to 4.21)	0.30
Aortic regurgitation*			-	0.48
None-trace	62/75 (82.7%)	59/68 (86.8%)		
Mild	13/75 (17.3%)	9/68 (13.2%)		
Moderate/Severe	0/75 (0%)	0/68 (0%)		
PPM (severe) VARC-2**	4/72 (5.6%)	7/68 (10.3%)	-4.74 (-13.69 to 4.21)	0.30
PPM (severe) VARC-3**	3/72 (4.2%)	5/68 (7.4%)	-3.19 (-10.29 to 4.55)	0.49

*The suboptimal quality of echocardiographic images precluded any evaluation of aortic regurgitation in 5 patients (TAVR: 1, SAVR: 4).
**The suboptimal quality of echocardiographic images precluded the evaluation of EOA (and subsequently the calculation of PPM) in 8 patients (4 patients in each group).

Valve Hemodynamics Over Time

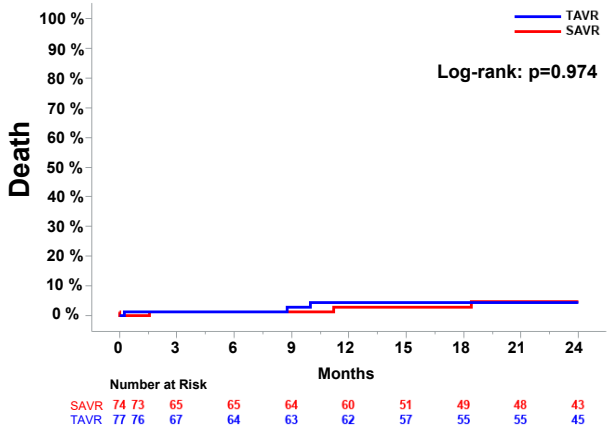


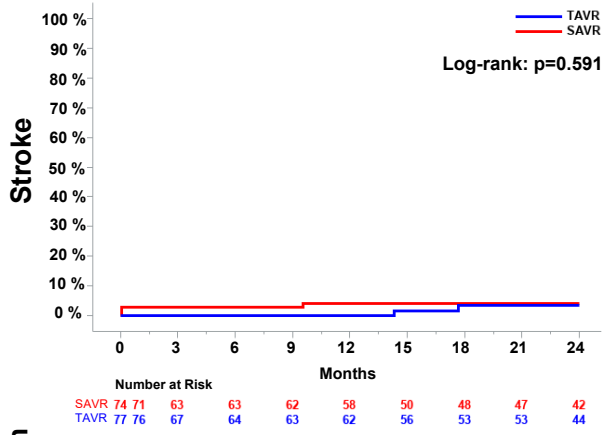
Follow-Up Outcomes
(median: 2 [1-4] years)

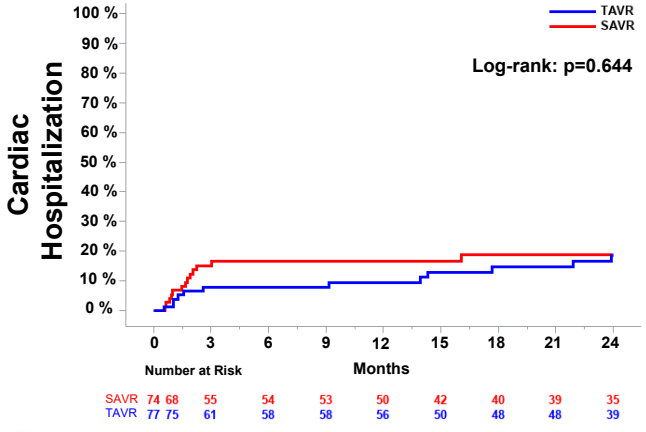
	TAVR (n= 77)	SAVR (n= 74)	TAVR vs SAVR (95%CI)†	*P* Value‡
Death	7 (9.1%)	6 (8.1%)	1.08 (0.36 to 3.22)	0.89
Stroke	3 (3.9%)	3 (4.1%)	0.95 (0.19 to 4.71)	0.95
Disabling stroke	0 (0%)	3 (4.1%)	0.14 (0.01 to 4.24)	0.26
Death or stroke	7 (9.1%)	8 (10.8%)	0.97 (0.70 to 1.34)	0.86
Myocardial infarction	2 (2.6%)	3 (4.1%)	0.68 (0.12 to 4.05)	0.68
Major/life-threatening bleeding	10 (13.0%)	18 (24.3%)	0.51 (0.24 to 1.11)	0.09
New-onset atrial fibrillation	8 (10.4%)	23 (31.1%)	0.30 (0.14 to 0.68)	<0.01
Permanent pacemaker	11 (14.3%)	5 (6.8 %)	2.07 (0.73 to 5.90)	0.17
Infective endocarditis	0 (0%)	2 (2.7%)	0.20 (0.01 to 8.07)	0.39
Aortic valve reintervention	2 (2.6%)	1 (1.4%)	1.10 (0.39 to 2.98)	0.88
Cardiac rehospitalization	15 (19.5%)	15 (20.3%)	0.91 (0.45 to 1.86)	0.80
Heart failure rehospitalization	4 (5.2%)	6 (8.1%)	0.64 (0.18 to 2.26)	0.49

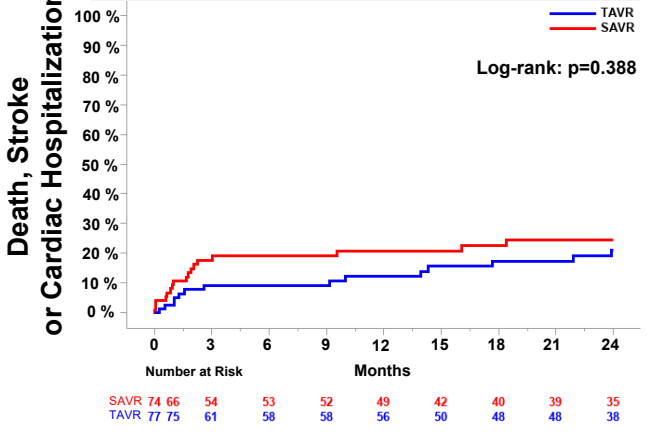
† Hazard ratio. ‡ Based on the log-rank test.

2-Year Follow-Up Outcomes

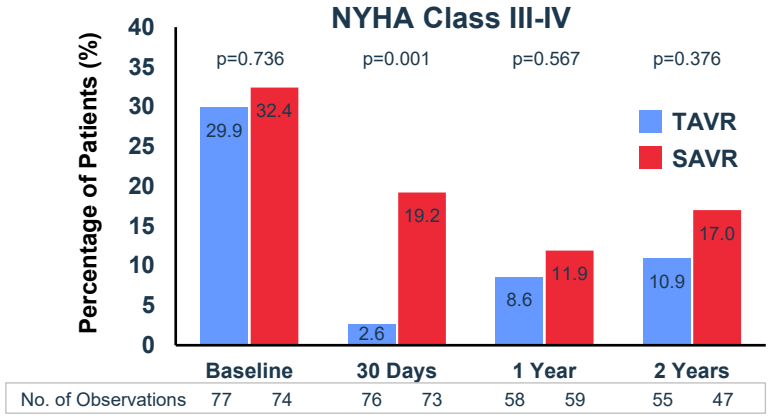


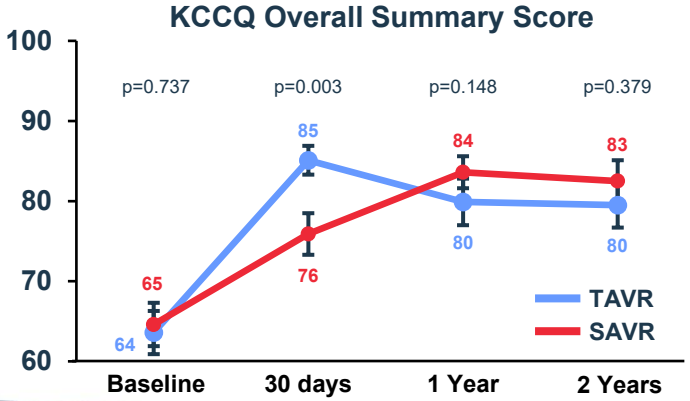


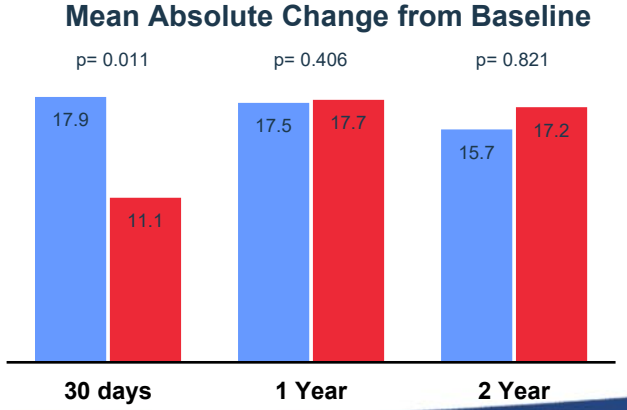




Functional Status – Quality of Life







Limitations

- Limited sample size: possibility of a type II error for some clinical variables.
- The early termination of the trial, along with the lower than expected rates of severe PPM, could have impacted the primary endpoint results of the study (underpowered trial).
- No clinical event adjudication committee.

Conclusions

- The vast majority of low-to-intermediate risk patients with aortic stenosis exhibiting the anatomic feature of SAA were women.
- In this challenging population, there was no evidence of contemporary TAVR superiority vs. SAVR regarding valve hemodynamic outcomes as evaluated by Doppler echocardiography, with relatively low rates of severe PPM in both groups.
- There were no significant differences between TAVR and SAVR in early and late (2-year) clinical outcomes.
- The results of this trial suggest that these 2 therapies represent a valid alternative for treating patients with aortic stenosis and small aortic annulus, and treatment selection should likely be individualized according to baseline characteristics, additional anatomical risk factors, and patient preference.