A sub-analysis of five-year outcomes from the COMMENCE aortic trial

Five-year comparison of clinical and echocardiographic outcomes of pure aortic stenosis with pure aortic regurgitation or mixed aortic valve disease in the COMMENCE aortic trial

Edwards

Clinical Summary:

Five-year comparison of clinical and echocardiographic outcomes of pure aortic stenosis with pure aortic regurgitation or mixed aortic valve disease in the COMMENCE aortic trial

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Objective

Mixed aortic valve disease (MAVD), defined as the combination of aortic stenosis (AS) and aortic regurgitation (AR), is a condition often associated with poorer outcomes than pure AS.

Surgical aortic valve replacement (SAVR) is a well-established treatment for patients with pure AS. However, clinical and echocardiographic outcomes in MAVD populations are less well understood. Additionally, the optimal timing for intervention remains unclear.

Key Outcomes

- Patients with pure AR + MAVD demonstrated similar clinical safety and SVD at 5 years compared to those with pure AS
- There was a significant difference in LV reverse remodeling in patients with pure AR
- These outcomes support treatment in patients with MAVD or AR before irreversible changes occur

Methods

- 458 patients from the FDA IDE COMMENCE SAVR trial with RESILIA tissue valves to 5 years were analyzed
- The primary outcome was all-cause mortality at 5 years. Secondary outcomes included reoperation, bleeding, endocarditis, structural (SVD) and non-structural (NSVD) valve deterioration, and changes in left ventricle (LV) variables

Patient Demographics

Inclusion Criteria

- Patients with pure AR + MAVD
  - Moderate or severe regurgitation at baseline with or without aortic stenosis
  - All patients in the MAVD group were investigated for pseudo-AS (peak velocity >2.0-2.5 m/s or AVA of >2.0 cm^2)
- Patients with pure AS
  - No regurgitation and mild, moderate, or severe stenosis at baseline

Key Demographics

	Pure AR + MAVD N=135	Pure AS N=323	p-value
Median age (years)	65.0	69.0	<.0001
Median STS score (%)	1.1	1.5	.0006
Mean gradient (mmHg)	21.4	33.6	<.0001
LVEDD (cm)	5.3	4.4	<.0001
LVESD (cm)	3.3	2.7	<.0001
LV mass (g)	266.3	215.7	<.0001
BSA corrected LV mass (g)	134.0	106.2	<.0001

Results

- Five-year freedom from all-cause mortality, reoperations, and major bleeding were not statistically different between groups [Figure 1]
  - No SVD or NSVD event occurred in either group [Table 1]

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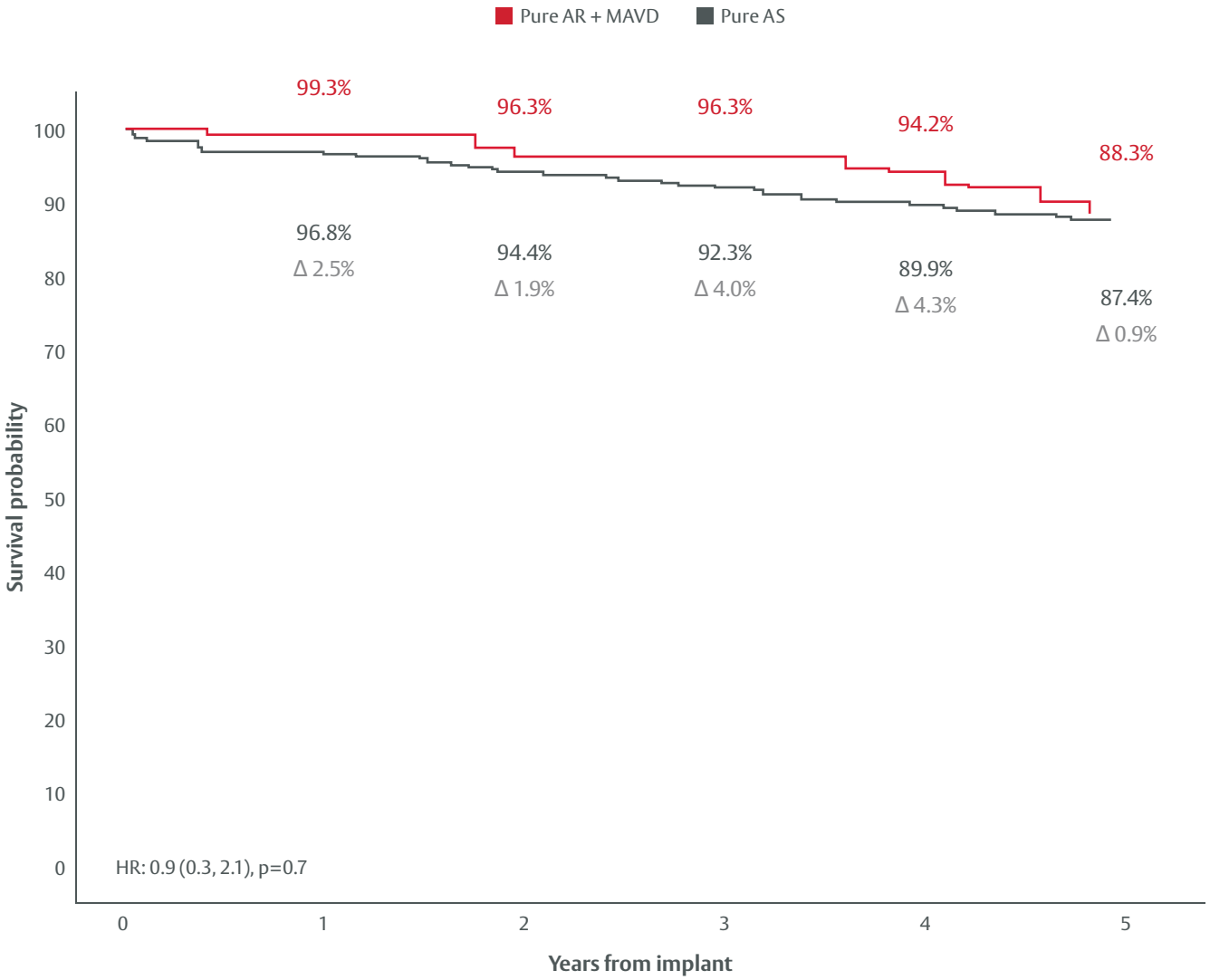
Results (cont.)

- Compared to patients with pure AS, patients with pure AR+MAVD had a greater change in LV mass regression, LVEDV, and LV end-diastolic dimension (LVEDD) [Table 2]
- Freedom from all-cause mortality for patients with pure AR was 96.3% through 5 years
- Patients with pure AR + MAVD with better LVEF at baseline (>55%) continued to demonstrate better LVEF at 5 years when compared to patients with poor LVEF (≤55%) at baseline

Conclusions

- In this IDE trial, patients with moderate to severe AR with or without AS demonstrated similar clinical safety outcomes over 5 years compared to patients with pure AS in the COMMENCE trial
- No reported SVD in any group through 5 years, clinically stable gradients, and similar freedom from all reoperations in both the groups (P = 0.43)
- Outcomes support the benefit of treatment in patients with MAVD or AR before irreversible changes occur

Figure 1. IPTW adjusted Kaplan-Meier plot



Results based on a synthetic pseudo-population generated by IPTW

Table 1. Adjusted safety endpoints (5 years)

Freedom from endpoint (%)	Pure AR + MAVD N=135	Pure AS N=323	p-value
All-cause mortality	88.3 ± 3.7	87.4 ± 2.1	0.67
All reoperations	97.9 ± 1.6	99.0 ± 0.7	0.43
All bleeding	91.5 ± 3.2	89.1 ± 2.1	0.61
• Major bleeding	96.1 ± 2.3	94.4 ± 1.5	0.53
Endocarditis	97.6 ± 1.7	97.5 ± 1.0	0.88
Paravalvular leak	100 ± 0	98.3 ± 0.8	0.21
SVD*	100 ± 0	100 ± 0	N/A
NSVD	100 ± 0	100 ± 0	N/A

Table 2. LV reverse remodeling (adjusted)

Variable	3 months		5 years		p-value (5 years)
	Pure AR + MAVD	Pure AS	Pure AR + MAVD	Pure AS	
LVEF (%)	64.15 (62.72, 65.57)	63.13 (62.20, 64.06)	63.23 (61.62, 64.85)	61.59 (60.48, 62.69)	0.11
Peak velocity (m/s)	2.03 (1.94, 2.12)	2.10 (2.04, 2.15)	2.06 (1.97, 2.15)	2.18 (2.11, 2.24)	0.06
LVESV (mL)	26.37 (24.20, 28.55)	29.31 (27.80, 30.82)	27.46 (25.03, 29.88)	30.37 (28.65, 32.09)	0.08
LV end systolic dimension (cm)	2.53 (2.41, 2.64)	2.68 (2.60, 2.75)	2.63 (2.49, 2.76)	2.99 (2.89, 3.09)	0.0001
LV end diastolic dimension (cm)	4.26 (4.13, 4.39)	4.45 (4.37, 4.53)	4.36 (4.21, 4.51)	4.64 (4.55, 4.73)	0.003
LV mass (g/m^2)	181.38 (170.85, 191.92)	191.63 (185.50, 197.77)	168.75 (158.32, 179.19)	182.32 (175.96, 188.67)	0.04
BSA corrected LV mass (g)	90.99 (86.24, 95.74)	95.13 (92.38, 97.88)	83.78 (79.07, 88.50)	90.42 (87.54, 93.33)	0.0

*All event definitions per CW Akins et al. which is based on reoperations J Thorac Cardiovasc Surg 2008; 135:732-8.

Important Safety Information:

INSPIRIS RESILIA Aortic Valve

Indications: For use in replacement of native or prosthetic aortic heart valves.

Contraindications: There are no known contraindications with the use of the INSPIRIS RESILIA aortic valve.

Complications and Side Effects: Thromboembolism, valve thrombosis, hemorrhage, hemolysis, regurgitation, endocarditis, structural valve deterioration, nonstructural dysfunction, stenosis, arrhythmia, transient ischemic attack/stroke, congestive heart failure, myocardial infarction, any of which could lead to reoperation, explantation, permanent disability, and death.

Warnings: DO NOT ADJUST THE VALVE DIAMETER BY EXPANDING THE BAND PRIOR TO OR DURING IMPLANTATION OF THE SURGICAL VALVE. The expandable band is not designed to allow for compression or expansion during implantation of the surgical valve. This will cause damage to the valve and may result in aortic incompetence. DO NOT PERFORM STAND-ALONE BALLOON AORTIC VALVULOPLASTY PROCEDURES ON THIS VALVE FOR THE SIZES 19 - 25 mm as this may expand the valve causing aortic incompetence, coronary embolism or annular rupture. Valve-in-valve sizing in the INSPIRIS valve has only been tested with specific Edwards transcatheter heart valves. Use of other transcatheter valves may result in embolization of transcatheter devices anchored within or result in annular rupture.

KONECT RESILIA Aortic Valved Conduit

Indications: For use in replacement of native or prosthetic aortic heart valves and the associated repair or replacement of a damaged or diseased ascending aorta.

Contraindications: There are no known contraindications with the use of the KONECT RESILIA aortic valved conduit.

Complications and Side Effects: Thromboembolism, valve thrombosis, hemorrhage, hemolysis, regurgitation, endocarditis, structural valve deterioration, nonstructural dysfunction, stenosis, arrhythmia, transient ischemic attack/stroke, congestive heart failure, myocardial infarction, any of which could lead to reoperation, explantation, permanent disability, and death. Adverse events potentially associated with the use of polyester vascular grafts include hemorrhage, thrombosis, graft infection, embolism, aneurysm, pseudoaneurysm, seroma, occlusion (anastomotic intimal hyperplasia), immunological reaction to collagen (shown to be a weak immunogen; infrequent, mild, localized and self-limiting), intimal peel formation, and conduit dilatation, any of which could lead to re-operation, explantation, permanent disability, and death.

CAUTION: Federal (USA) law restricts these devices to sale by or on the order of a physician. See instructions for use for full prescribing information.

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