Transcatheter Aortic Valve Replacement in Low Risk Patients with Bicuspid Aortic Stenosis

1-year results from the LRT trial

Dr. Toby Rogers, MD, PhD[1,2] on behalf of the LRT investigators

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Disclosures

- Consultant and physician proctor: Edwards Lifesciences, Medtronic
- Advisory board: Medtronic
- Equity interest: Transmural Systems

- LRT was supported by MedStar Health Research Institute, participating sites, and Medtronic

LRT trial (NCT02628899)

Design:	Prospective, multicenter, registry
Primary endpoint:	All cause mortality at 30 days
Secondary endpoints:	Safety and efficacy
	Clinical outcomes (VARC-2)
	Valve hemodynamics by echocardiography
	Subclinical leaflet thrombosis evaluation by CT at 30 days
Enrollment period:	August 2016 – February 2020s

JACC: CARDIOVASCULAR INTERVENTIONS
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AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION

VOL. 13, NO. 9, 2020

LOW RISK TAVR

FOCUS ON TRANSCATHETER AORTIC VALVE REPLACEMENT

Transcatheter Aortic Valve Replacement in Low-Risk Patients With Symptomatic Severe Bicuspid Aortic Valve Stenosis

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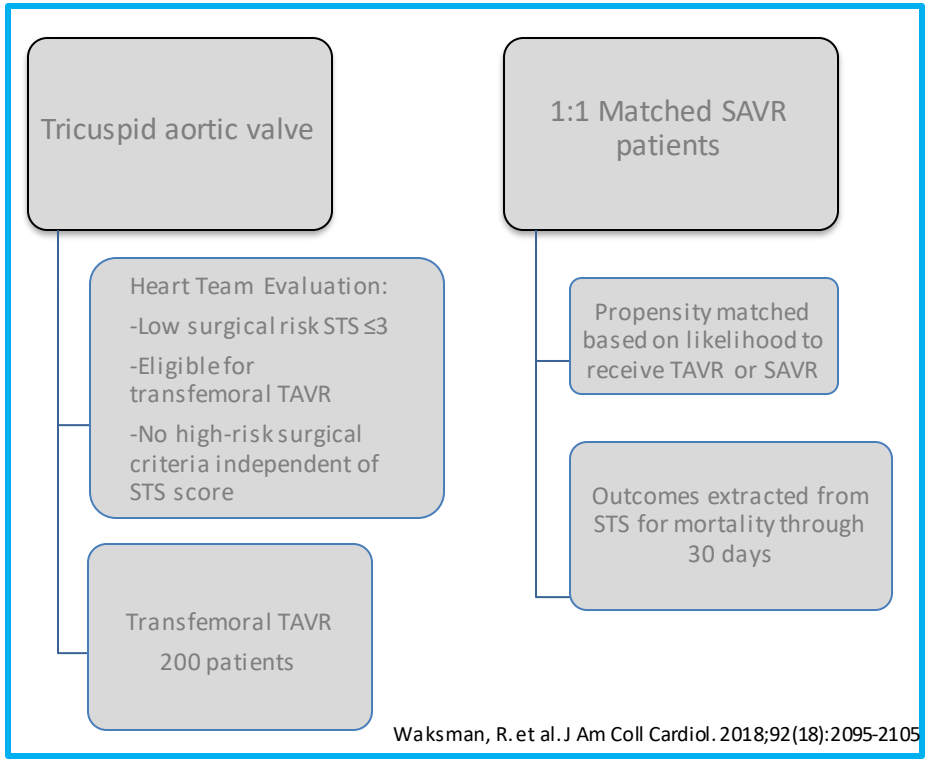
Waksman et al. JACC Cardiovasc Interv, 2020, 13(9):1019-1027.

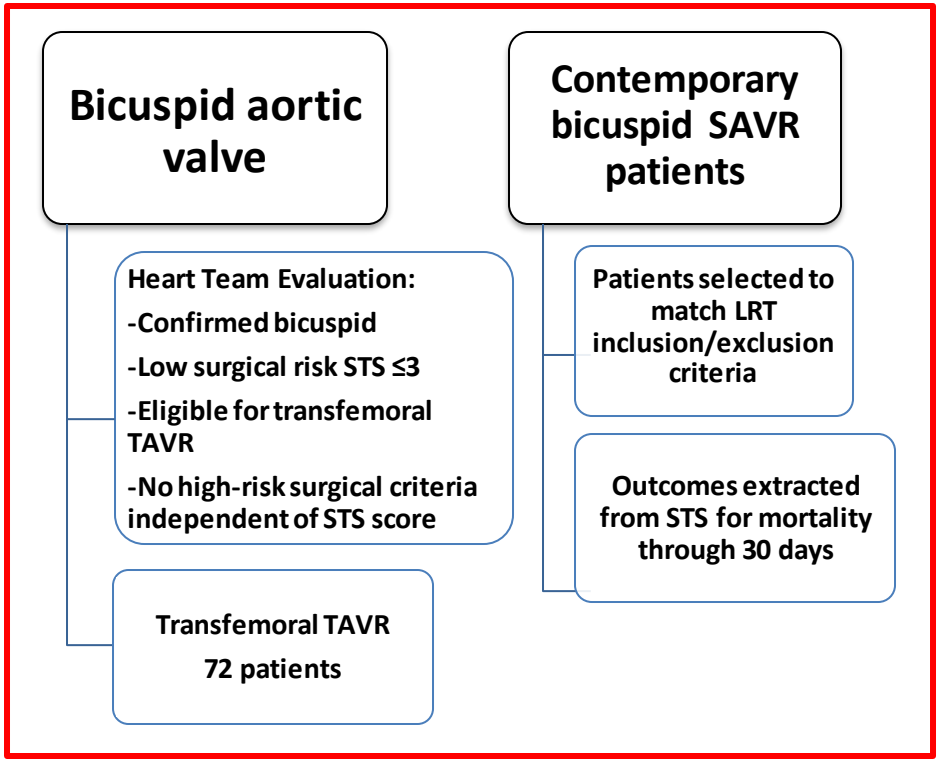
LRT bicuspid cohort objective

To assess the feasibility of TAVR with commercially available valves in low-risk bicuspid patients with symptomatic, severe aortic stenosis

LRT study design



Waksman, R. et al. J Am Coll Cardiol. 2018;92(18):2095-2105



Trial administration

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Christian Shults, MD, FACS, FACC (Cardiothoracic Surgery)

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Director CT Core Lab
Gaby Weissman, MD

Independent Clinical Events Committee
Chairman
Hector Garcia-Garcia, MD

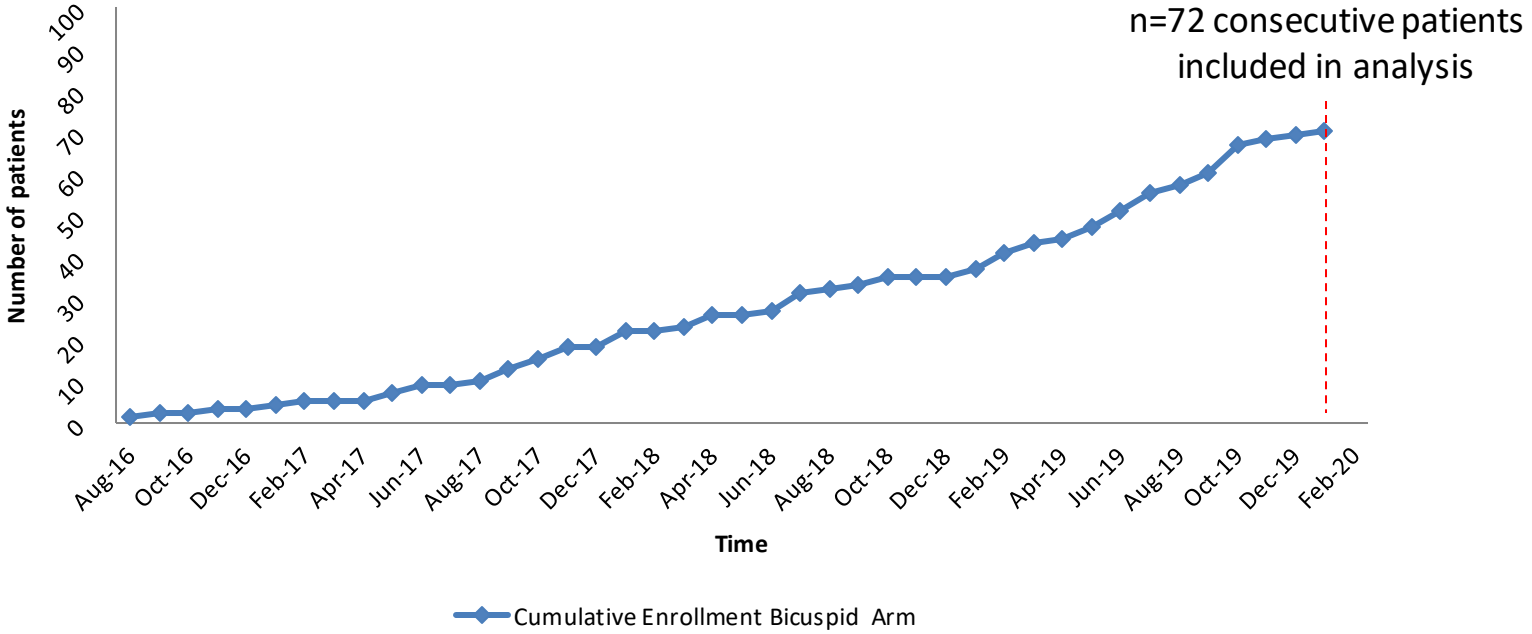
Database Technology
Director
Alan Monath

Data & Safety Monitoring Board
Chairman
William Weintraub, MD

Enrolling sites

Site Name	Principal Investigators	Location
MedStar Washington Hospital Center	Ron Waksman, MD Christian Shults, MD	Washington, DC
Miriam Hospital	Paul Gordon, MD Afshin Ehsan, MD	Providence, RI
Stony Brook Hospital	Puja Parikh, MD Thomas Bilfinger, MD	Stony Brook, NY
Henrico Doctors' Hospital	Robert Levitt, MD Chiwon Hahn, MD	Richmond, VA
Sutter Health System	David Roberts, MD Michael Ingram, MD	Sacramento, CA
St. John Heart Institute	Nicholas Hanna, MD George Comas, MD	Tulsa, OK
Wellstar Health System	Amar Patel, MD William Cooper, MD	Marietta ,GA

Bicuspid enrollment timeline



Key inclusion/exclusion criteria

Key inclusion criteria

- Symptomatic severe AS of a bicuspid aortic valve
- Low risk according to the multidisciplinary Heart Team
- STS PROM ≤ 3%
- Suitable for transfemoral access with commercial TAVR device
- Life expectancy ≥ 1 year

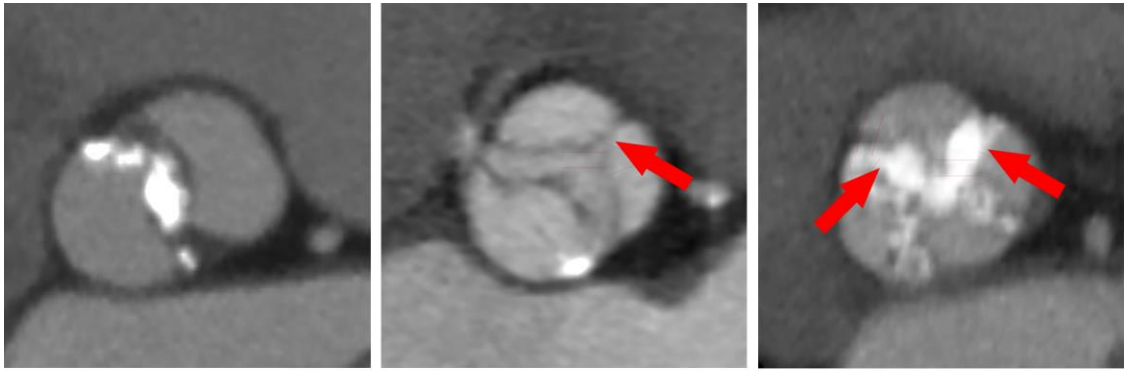
Key exclusion criteria

- Tricuspid aortic valve
- Frailty
- Severe CAD
- Severe other valve disease
- Prior heart surgery
- Recent stroke or MI
- Severe lung disease
- Severe renal failure
- Porcelain Aorta
- Severe Disease not captured in STS
- Alternative access to femoral

Baseline characteristics

Mean ± standard deviation or n/N (%)	Bicuspid TAVR	Bicuspid SAVR	Tricuspid TAVR
Age, years	68.1±7.7	63.4±8.2	74.1±6.1
Male	33/72 (45.8%)	142/216 (65.7%)	123/200 (61.5%)
NYHA class III or IV	15/72 (20.8%)	34/215 (15.8%)	35/200 (17.5%)
STS-PROM score †, %	1.4±0.6	1.1±0.5	1.8±0.5
Diabetes mellitus	9/72 (12.5%)	41/216 (19%)	61/200 (30.5%)
Renal insufficiency	2/72 (2.8%)	4/213 (1.9%)	12/200 (6.0%)
Hypertension	45/72 (62.5%)	150/216 (69.4%)	171/200 (85.5)
Prior stroke or TIA	5/72 (6.9%)	17/216 (7.9%)	19/200 (9.5%)
Chronic lung disease	6/72 (8.3%)	37/216 (17.1%)	16/200 (8.0%)
LVEF	63.5±9.8	57.7±9.1	63.5±7.4
Prior PCI	2/72 (2.8%)	11/216 (5.1%)	42/200 (21.0%)
Prior CABG	0/72 (0.0%)	3/216 (1.4%)	2/200 (1.0%)
Pre-existing PPM	1/72 (1.4%)	2/212 (0.9%)	7/200 (3.5%)
Prior myocardial infarction	2/72 (2.8%)	7/214 (3.3%)	12/200 (6.0%)

Sievers classification



Sievers Type 0
(14.0%)

Sievers Type 1
(82.5%)

Sievers Type 2
(3.5%)

Red arrows indicate fused raphes in Sievers type 1 and 2 bicuspid morphologies

Sievers et al. J Thorac Cardiov Surg. 2007;133:1226-33

Pre-TAVR CT analysis

Mean ± standard deviation or n(%)	Bicuspid TAVR
Sievers classification	
Sievers type 0	10/70 (14.2%)
Sievers type 1 (fused raphe)	49/70 (70.0%)
Sievers type 2 (two fused raphes)	3/70 (4.3%)
Sievers type uncertain*	8/70 (11.4%)
Aortic annulus	
Max diameter, mm	28.2±2.8
Min diameter, mm	22.6±2.8
Coronary arteries	
Left coronary height, mm	13.6±3.7
Right coronary height, mm	16.1±3.9
Ascending aorta max diameter, mm	36.9±4.5

* Uncertain most commonly due to poor image quality

Procedural details

Mean ± standard deviation or n/N (%)	Bicuspid TAVR
Total procedure time, min	91.7±33.0
General anesthesia	15/71 (21.1%)
Transfemoral access	72/72 (100.0%)
Pre-dilatation	62/64 (96.9%)
Transcatheter heart valve type	
Balloon-expandable valve	48/72 (66.7%)
Self-expanding valve	24/72 (33.3%)
Implantation of >1 valve	
Conversion to surgery	
Hospital length of stay (days)	2.4±1.4

Valve size implanted	Bicuspid TAVR
20mm	0/72 (0.0%)
23mm	14/72 (19.4%)
26mm	28/72 (38.9%)
29mm	24/72 (33.3%)
34mm	6/72 (8.3%)
Valve size implanted	**Bicuspid SAVR**
≤19mm	7/216 (3%)
21mm	50/216 (23%)
23mm	92/216 (43%)
25mm	51/216 (24%)
27mm	12/216 (6%)
29mm	4/216 (1%)

Primary endpoint

***Zero* mortality at 30 days**

Waksman et al. JACC Cardiovasc Interv, 2020, 13(9):1019-1027.

1 year clinical outcomes

Outcome (%)	Bicuspid TAVR*	Bicuspid SAVR†	Tricuspid TAVR
All-cause death	1/67 (1.5%)‡	—	6/197 (3.0%)
Acute kidney injury	0/66 (0.0%)	—	0/200 (0)
Stroke	3/66 (4.5%)§	—	4/191 (2.1%)
Acute myocardial infarction	0/66 (0.0%)	—	2/191 (1.0%)
Endocarditis	0/66 (0.0%)	—	2/191 (1.0%)
New-onset atrial fibrillation	2/66 (3.0%)	—	12/191 (6.3%)
New PPM implantation	9/66 (13.6%)	—	14/193 (7.3%)

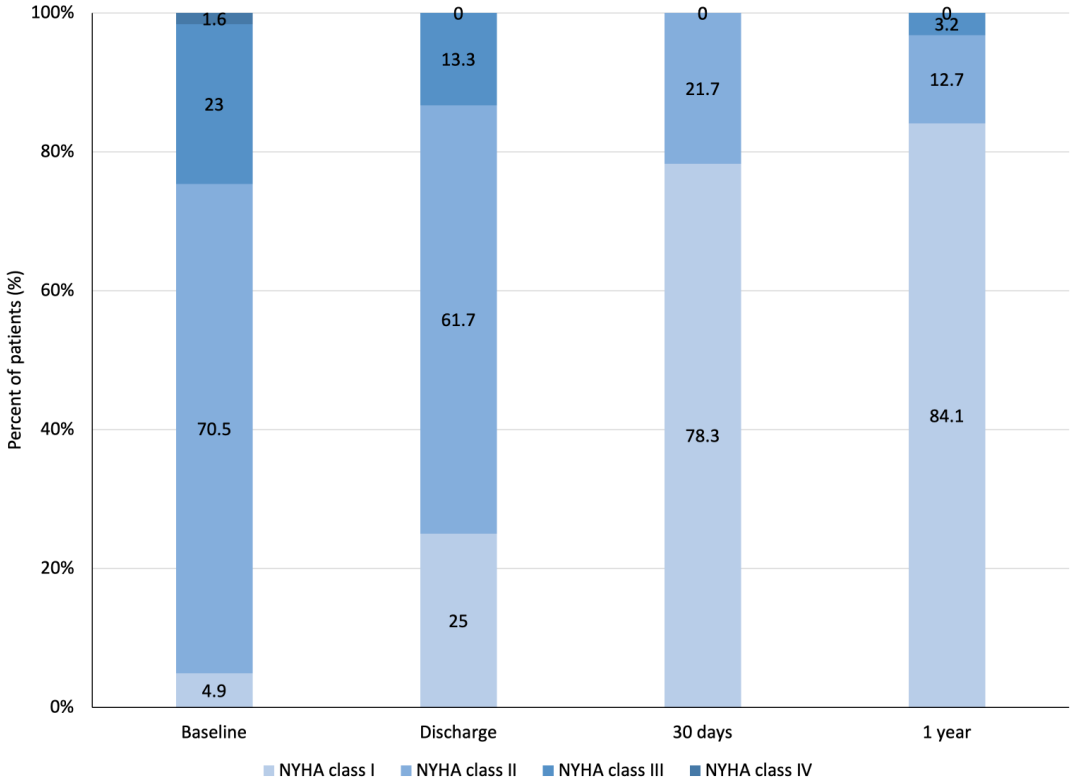
* n=3 patients lost to follow-up, n=1 withdrew consent, n=1 not yet reached 12-month follow up window

† SAVR outcomes obtained from STS database, which does not collect data beyond 30-days

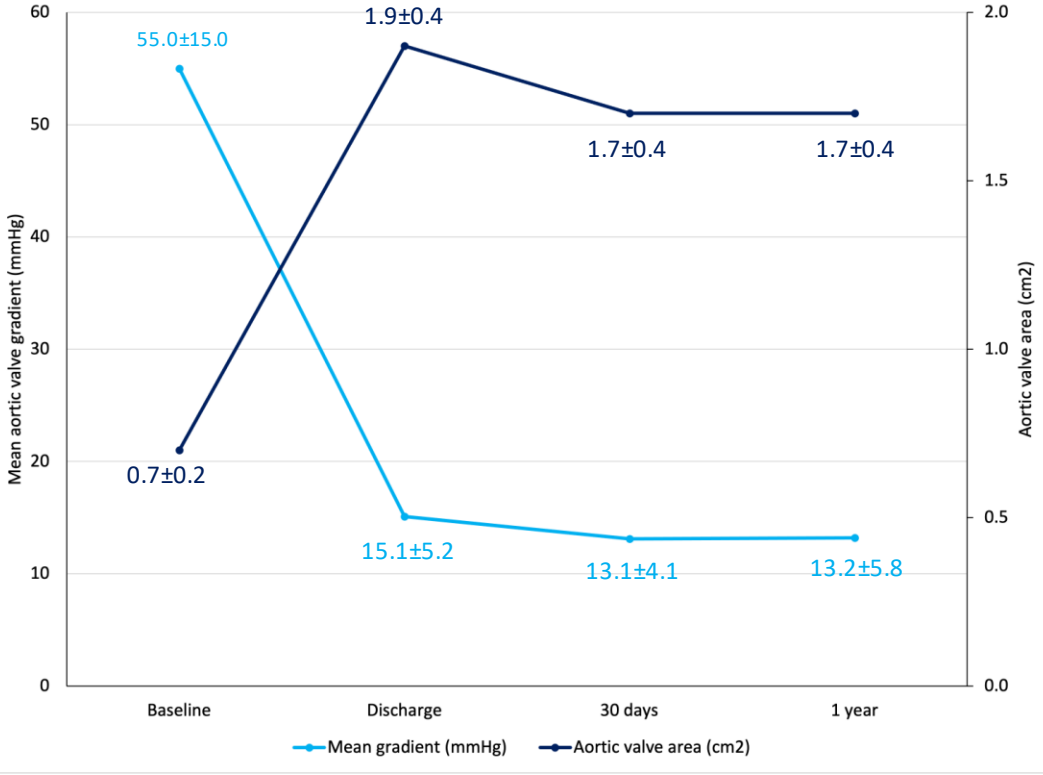
‡ Sudden death 291 days after TAVR, no post-mortem performed

§ All strokes were non-disabling

NYHA class in bicuspid cohort

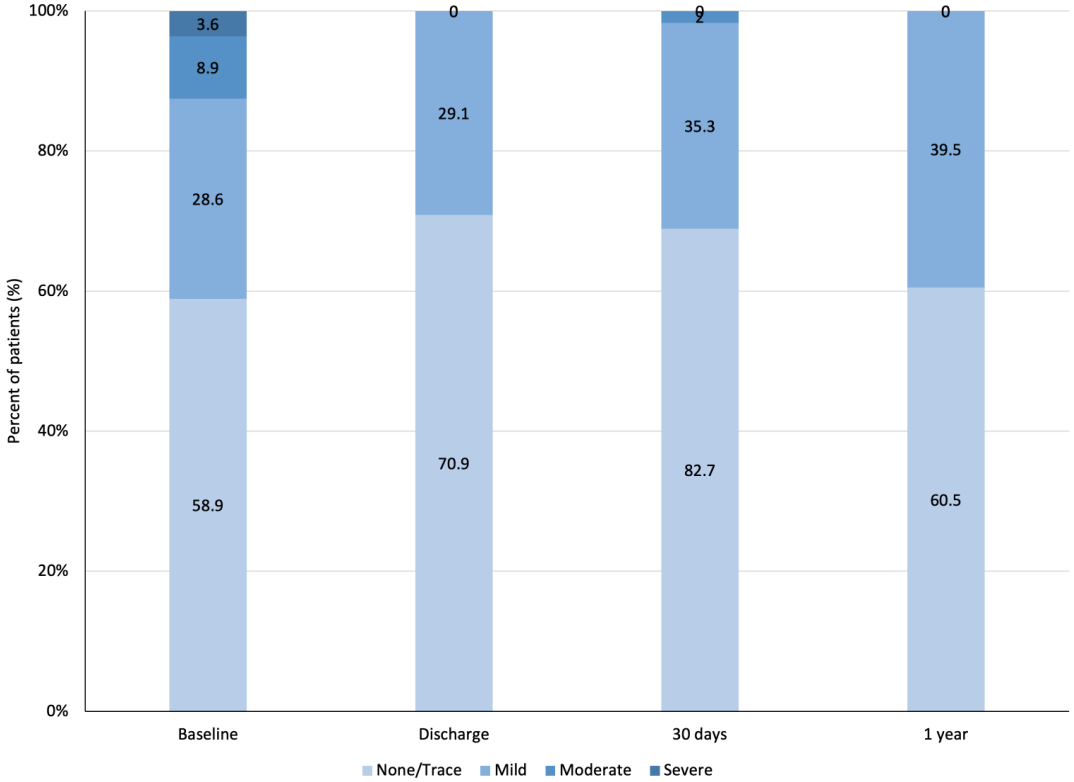


Hemodynamics*



*Core lab adjudicated

Paravalvular aortic regurgitation*



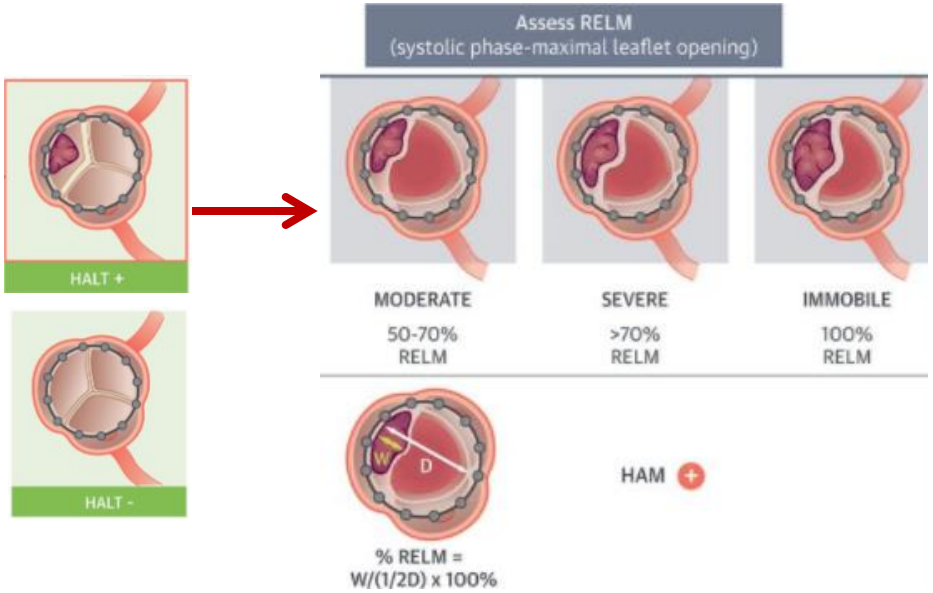
*Core lab adjudicated

Subclinical leaflet thrombosis

HALT: Hypo-**A**ttenuating **L**eaflet **T**hickening

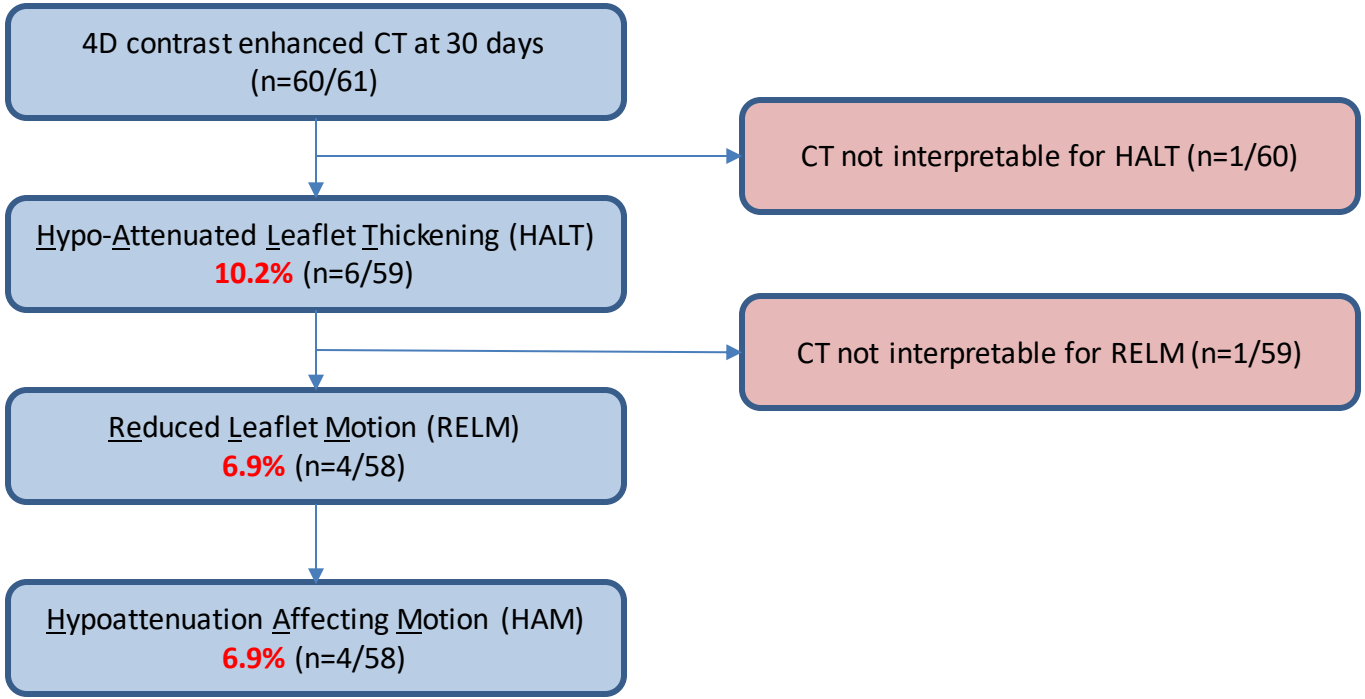
RELM: Reduced **L**eaflet **M**otion

HAM: Hypo-**A**ttenuation affecting **M**otion



Jilaihawi et al. JACC Cardiovasc Img, 2017, 10(4):461-70.

Subclinical leaflet thrombosis*



*Core lab adjudicated

Conclusions

1. Low-risk patients with bicuspid AS were younger than patients with tricuspid AS
2. Only a minority of patients had Sievers Type 0 morphology
3. Clinical outcomes and TAVR valve hemodynamics remained excellent at 1 year
4. Subclinical leaflet thrombosis rate was similar to patients with tricuspid AS

Thank you to all of the patients, site personnel, investigators, and FDA who made the LRT trial possible!