

One-Year Outcomes from the COMPASSION S3 Post-Approval Study (PAS)

Treatment of Patients with a Dysfunctional Right Ventricular Outflow
Tract Conduit or Previously Implanted Pulmonic Valve with the
SAPIEN 3 Transcatheter Heart Valve

Gregory Fleming, MD on behalf of the
CS3 PAS Investigators

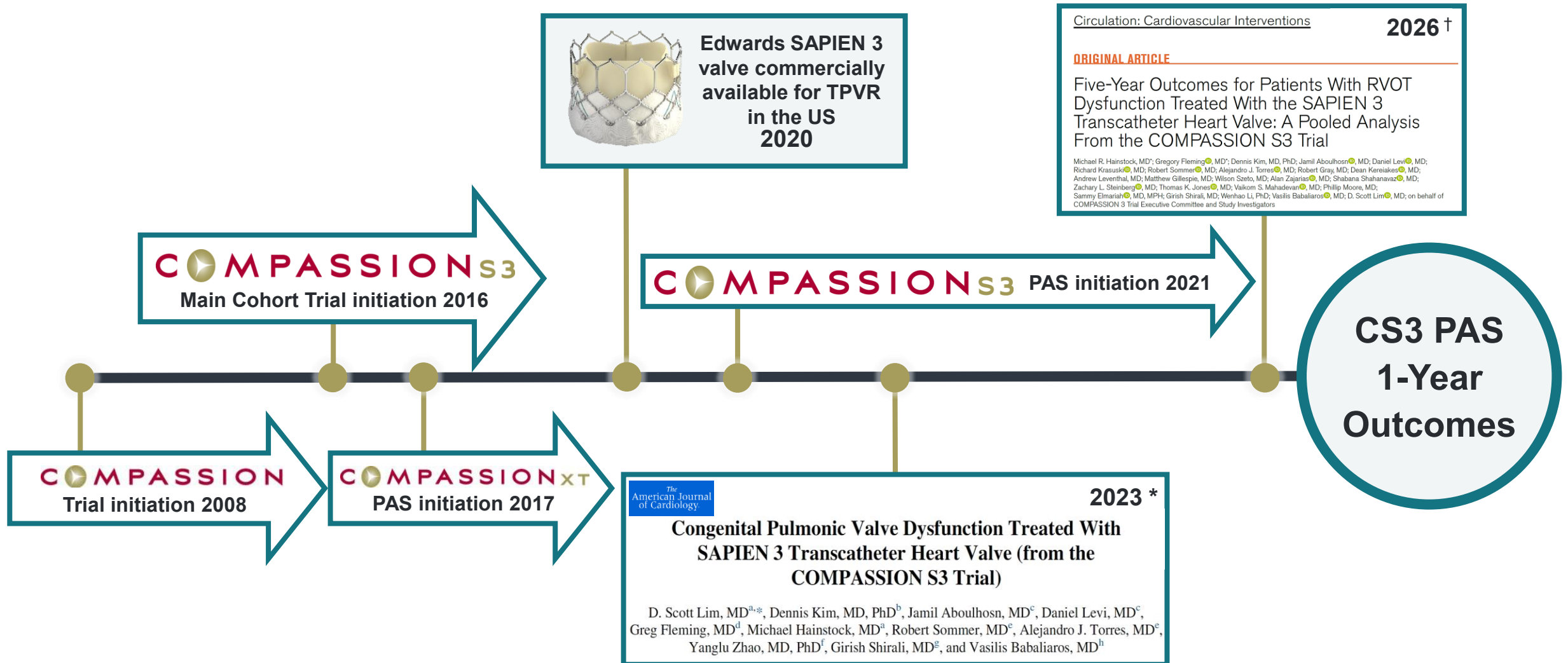
COMPASSION S3

Disclosures

As a faculty member for this program, I disclose the following relationships with industry:

- Consultant for PECA Labs Inc.
- Principal Investigator for Medtronic and Edwards Lifesciences

The COMPASSION Trials



COMPASSION_{S3}

*Lim et al., Am J Cardiol 2023; 190:102-109. †Hainstock et al., Circ Interventions 2026; 19:401-412.

COMPASSION S3 Pivotal to PAS

Pivotal Trial

Prospective, single-arm

 **58** Patients



Up to 12 US Sites



Echo core lab, CEC, DSMB



Discharge, 30D, 6M, annually through 5Y



Initiation prior to regulatory approval

Post-Approval Study

Prospective, single-arm

 **150** Patients



Up to 20 US sites



Echo core lab, CEC



Discharge, 30D, annually through 5Y



Conducted in post-approval setting



SCALE

58 → 150
patients



EVIDENCE CONTINUITY

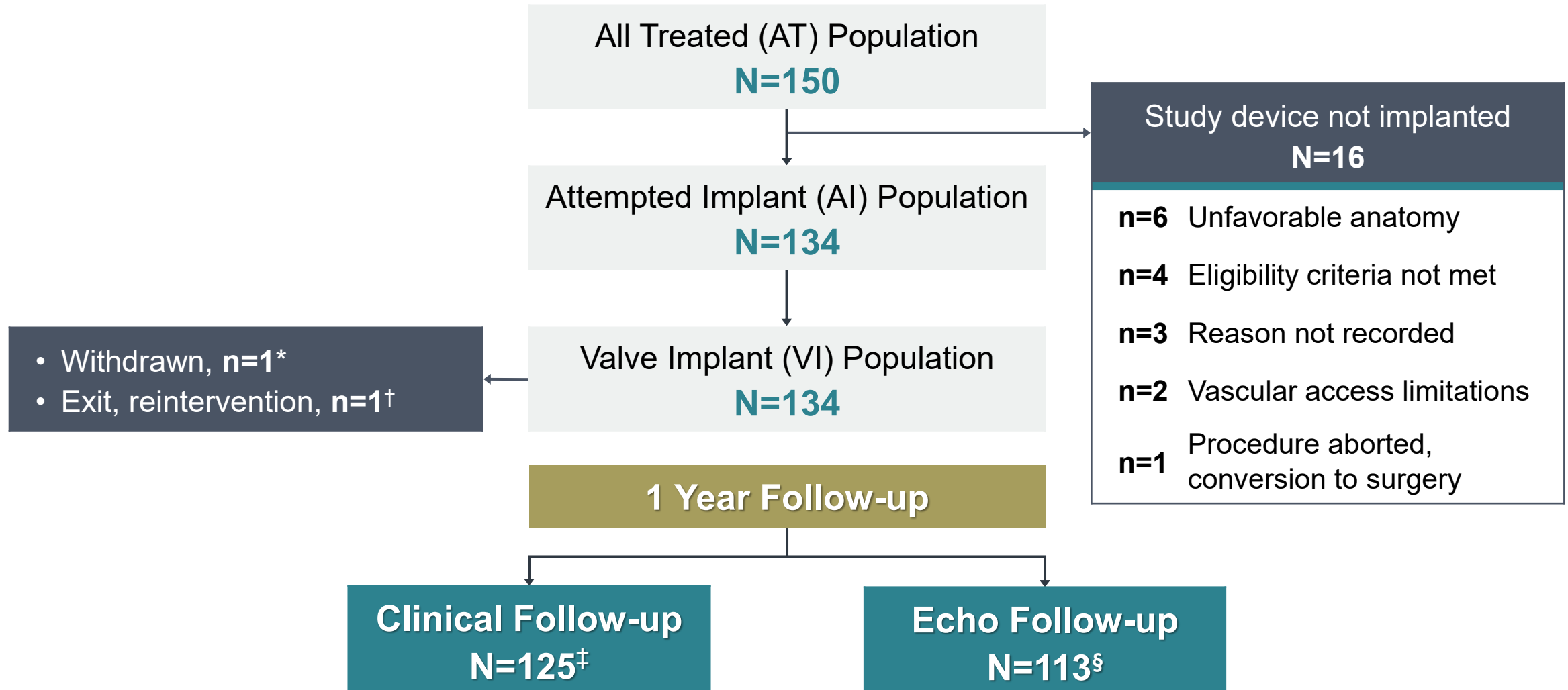
Core lab + CEC



CLINICAL USE

Protocol → IFU
Approved
regulatory use

Patient Flow



*Withdrawn for medical reason. †One patient underwent RVOT reintervention and exited before the 1-year follow-up.

‡Patients alive, on study and completed the scheduled follow-up visit. §Patients with key readable echoes for at least one parameter at 1 year.

Baseline Characteristics

Variable	Summary Statistics (N=150)
Age, years	30.3 ± 14.2
< 12 years	2.7% (4/150)
12-21 years	27.3% (41/150)
> 21 years	70.0% (105/150)
Female sex	42.0% (63/150)
Weight (kg)	74.2 ± 23.6
Height (cm)	165.0 ± 14.3
Primary Indication per Site	
PS alone	8.1% (12/148)
PR alone	16.2% (24/148)
PS + PR	75.7% (112/148)

Variable	Summary Statistics (N=150)
Total PR per Core Lab	
≤ Mild	15.0% (21/140)
≥ Moderate	85.0% (119/140)
Pulmonary Stenosis per Core Lab*	
Mild	26.6% (38/143)
Moderate	51.7% (74/143)
Severe	21.7% (31/143)
NYHA class III/IV	21.6% (32/148)
Most recent RVOT/PV Repair/Replacement	
Homograft/valved conduit	36.0% (54/150)
Bioprosthetic heart valve	61.3% (92/150)
Other†	2.7% (4/150)

*Stratified according to the EAE/ASE 2009 Echocardiographic assessment of valve stenosis.

†Synthetic conduit (n=1), Pericardial/Transannular patch (n=1), Valvuloplasty (Prior SHV) (n=2). Data are mean ± SD or % (n/N).

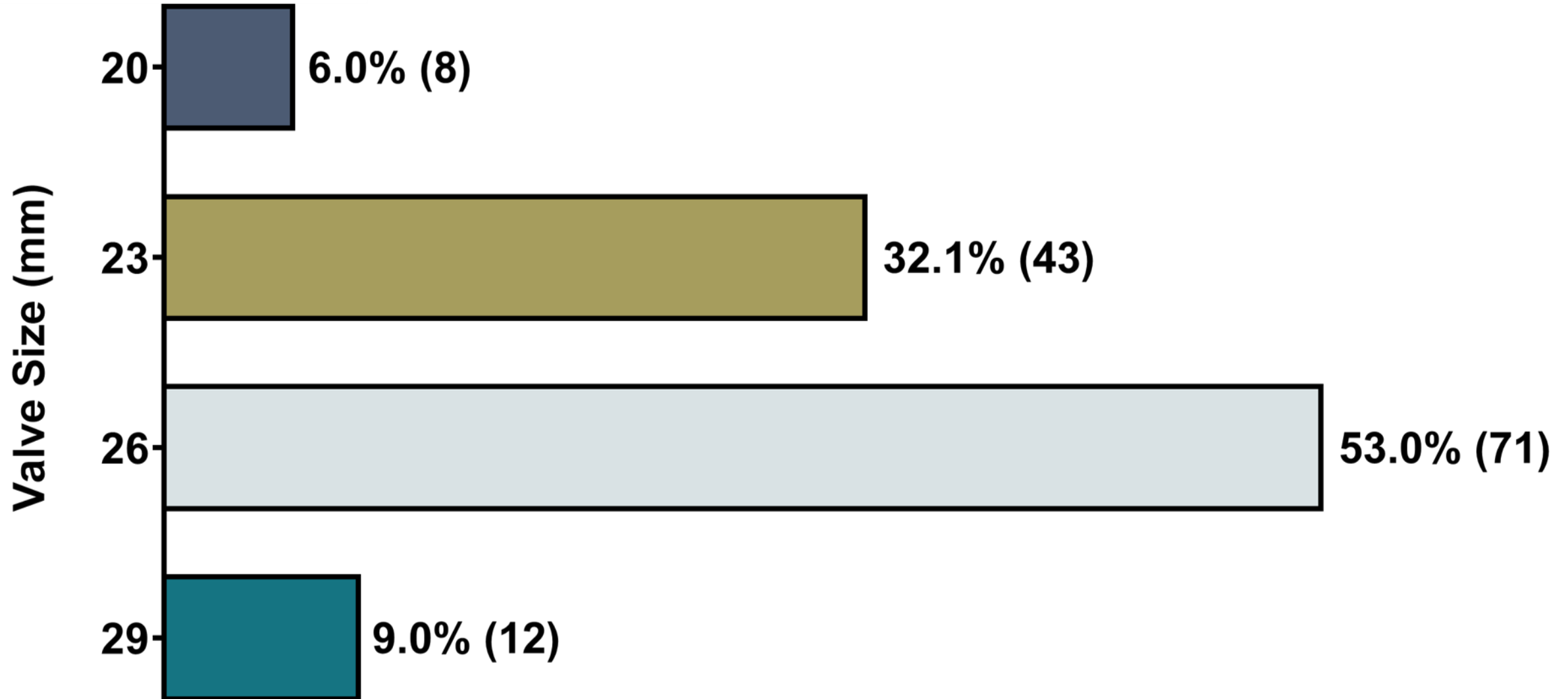
Procedural Information

Variable	Summary Statistics (N=150)
Catheter Laboratory Time, min	194.0 ± 77.7
Procedure Time, min	118.2 ± 70.4
Anesthesia	
General	96.7% (145/150)
Conscious Sedation	2.7% (4/150)
Conscious to General Conversion	0.7% (1/150)

Variable	Summary Statistics (N=150)
Pre-Dilatation	81.2% (121/149)
Pre-Stenting	20.0% (30/150)
Post-Dilatation	22.4% (30/134)
Valve not fully expanded	21
Paravalvular leak	2
Other*	7
Procedure Aborted†	0.7% (1/150)
Second SAPIEN 3 Implanted‡	0.7% (1/134)

*Residual gradient (n=2), physician decision (n=2), possible stuck valve leaflet (n=1), residual recoil/pre-stent (n=1), unspecified (n=1). †One procedure aborted due to conduit rupture during balloon dilatation; patient was converted to emergent surgical RV-PA conduit replacement prior to study device implantation. ‡A second 23 mm valve was implanted after post-dilatation due to incomplete expansion of the initial valve and moderate PR. Echo Core Lab assessment demonstrated no PR at 30 days or 1 year.

SAPIEN 3 Valve Distribution



Outcome: Device Success

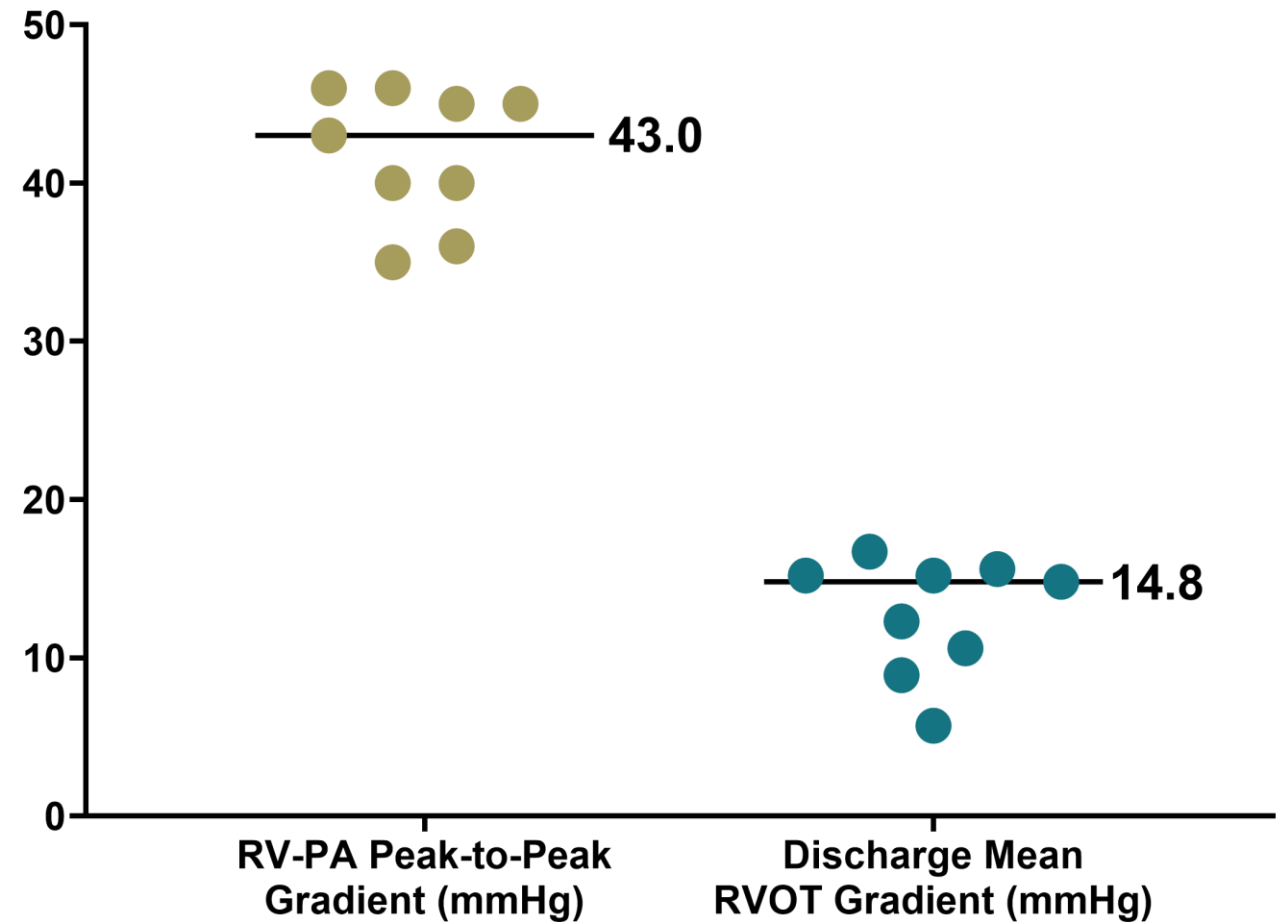
Event	Summary Statistics N=134
Device Success	90.8% (119/131)
Single THV implanted in the desired location [*]	99.3% (133/134)
RV-PA peak-to-peak gradient < 35 mmHg [†]	93.2% (124/133)
Less than moderate PR by discharge TTE	98.5% (130/132)
Free of explant at 24 hours post implantation	100.0% (134/134)

^{*}One patient received a second valve to treat moderate PR following post-dilatation. [†]Site-reported intra-procedural outcome.

RV-PA Peak-to-Peak Gradient ≥ 35 mmHg

RV-PA Peak-to-Peak Gradient (mmHg)*	Discharge Mean RVOT Gradient (mmHg)†
35.0	12.3
36.0	15.2
40.0	5.7
40.0	10.6
43.0	8.9
45.0	14.8
45.0	15.2
46.0	15.6
46.0	16.7

*Site-reported intra-procedural outcome. †Echo core lab data.



Outcome: THV Dysfunction at 1 Year

Event	Summary Statistics N=134
THV Dysfunction	1.8% (2/111)
RVOT Reintervention*	0.7% (1/134)
Moderate or Greater PR	0.9% (1/112)
Mean RVOT Gradient > 40 mmHg	0.0% (0/111)

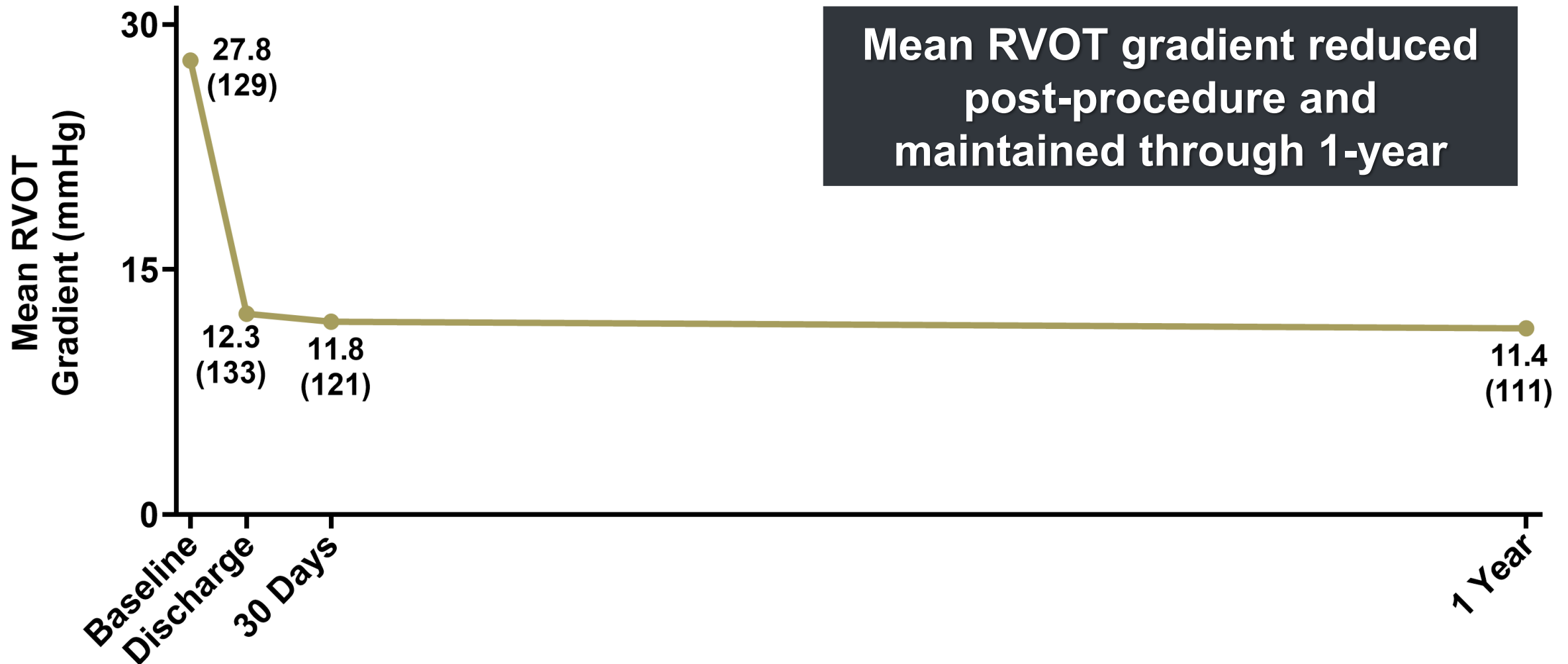
**One patient underwent RVOT reintervention due to severe PR by discharge TTE. The patient exited the study on POD 126 prior to the 1-year visit.*

Other Clinical Outcomes

Event (N=134)	30 Days	1 Year
Death	0.0% (0)	0.0% (0)
RVOT Reintervention*	0.0% (0)	0.8% (1)
Arrhythmia	1.5% (2)	3.8% (5)
Permanent Pacemaker	0.0% (0)	0.8% (1)
Endocarditis†	0.0% (0)	0.8% (1)
Pulmonary Embolism	0.0% (0)	0.0% (0)
Stroke or TIA	0.0% (0)	0.0% (0)
Prosthetic Valve Thrombosis‡	0.0% (0)	1.5% (2)
Major Bleeding	0.0% (0)	-
Major Vascular Injury	0.0% (0)	-
Major Access Site Complication	0.0% (0)	-

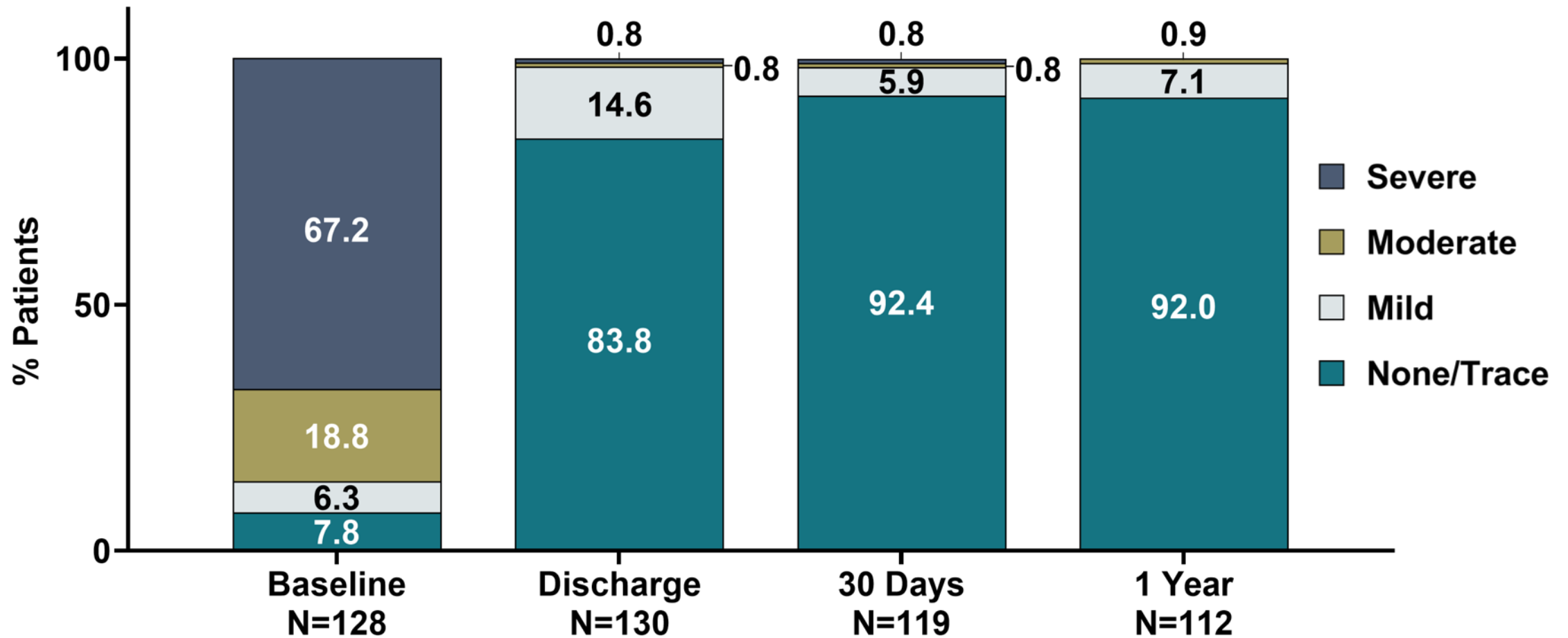
*CEC adjudicated RVOT reintervention due to severe PR by discharge TTE; patient exited on POD 126. †CEC adjudicated endocarditis with severe biventricular failure requiring VA-ECMO; patient transferred for VAD/transplant evaluation and withdrawn on POD 297. ‡Thrombosis is a site-reported event.

Mean RVOT Gradient



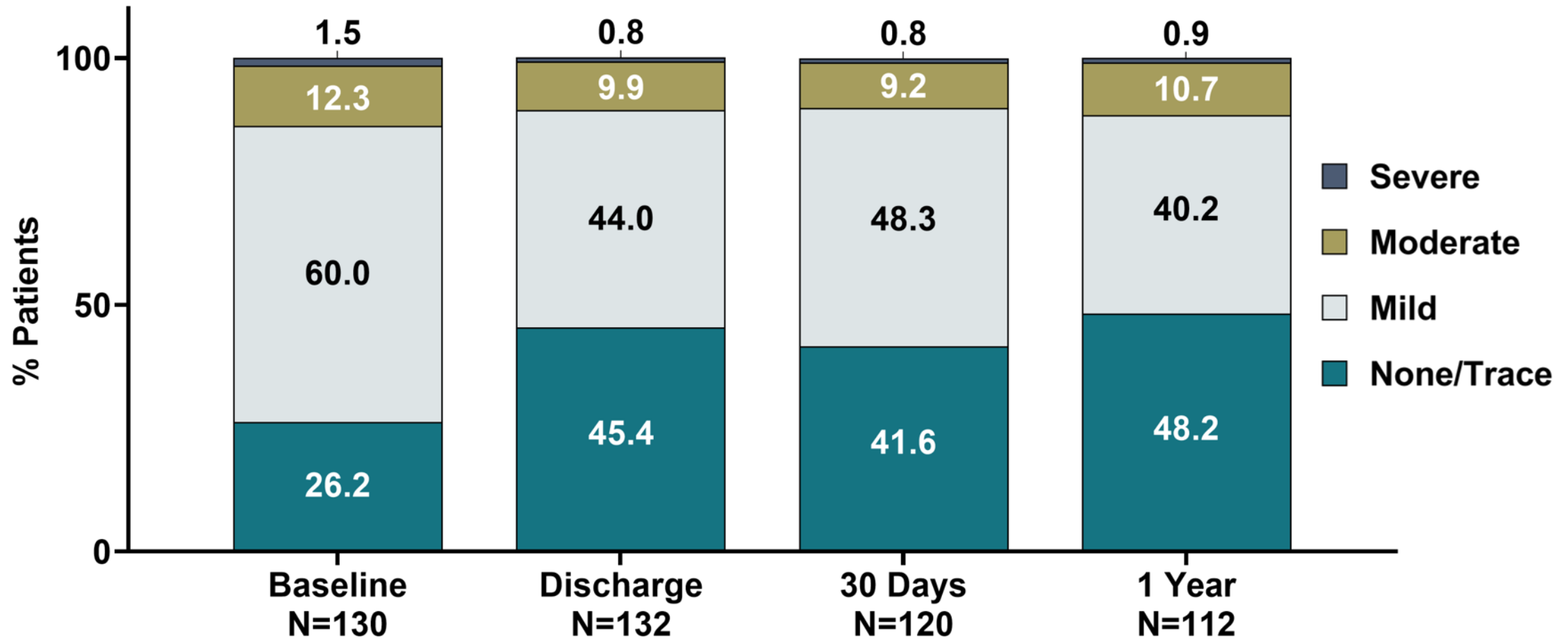
Total Pulmonary Regurgitation

92.0% of patients had none/trace total PR at 1 year



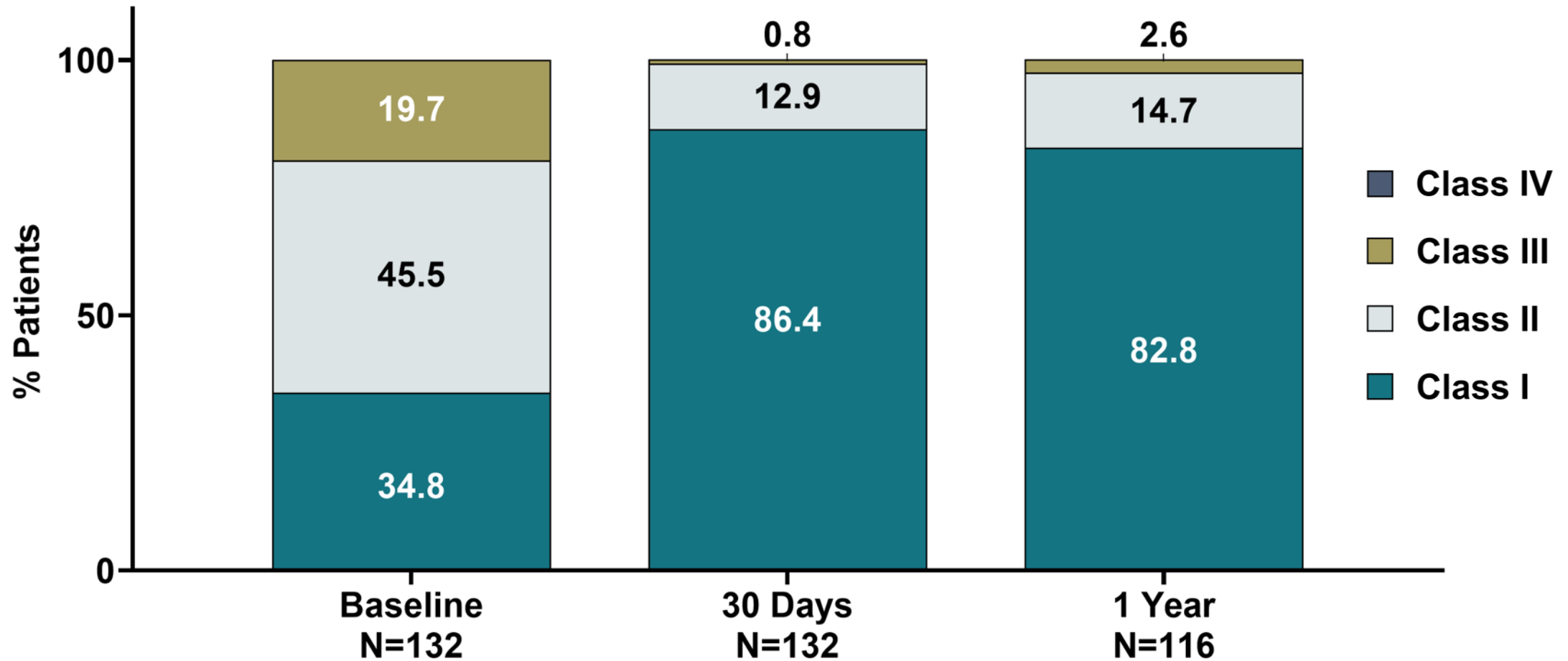
Tricuspid Regurgitation

88.4% none/trace or mild tricuspid regurgitation at 1 year

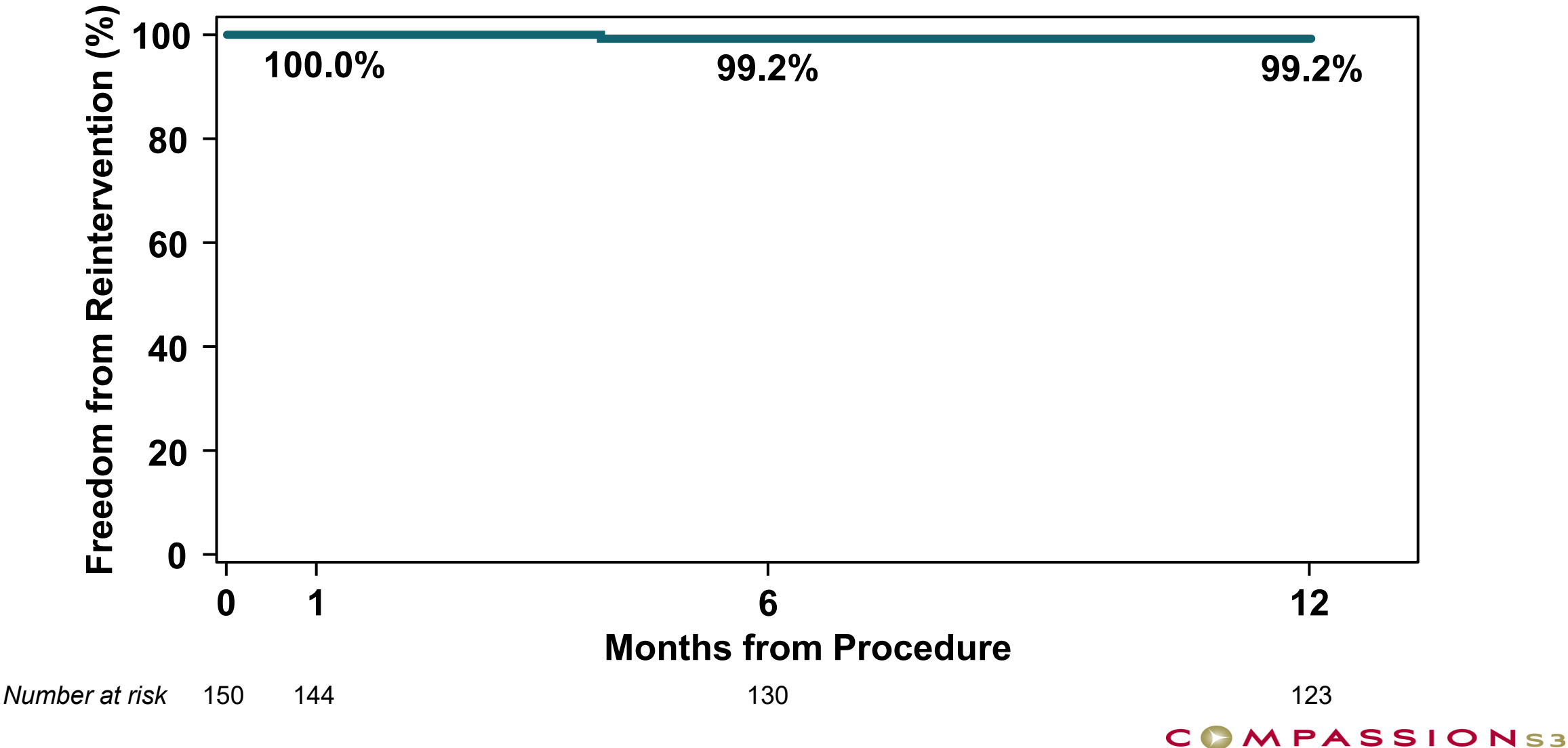


NYHA Functional Class

Sustained functional improvement through 1 year

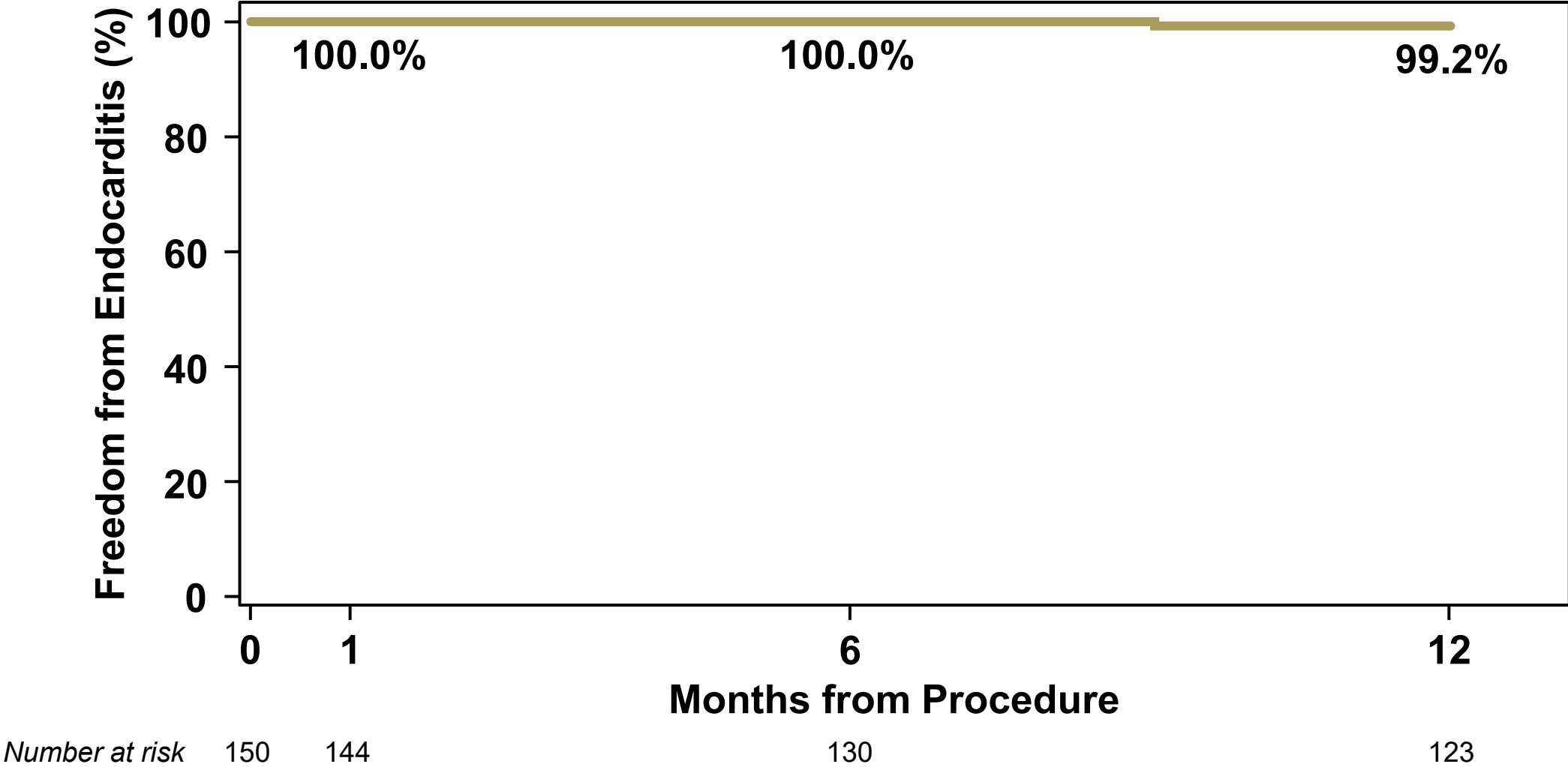


Freedom from Reintervention



All treated population (N=150). One CEC-adjudicated RVOT reintervention due to severe PR by discharge TTE. The patient exited the study on POD 126 prior to the 1-year visit.

Freedom from Endocarditis



All treated population (N=150). One CEC-adjudicated endocarditis event; patient transferred for VAD/transplant evaluation and withdrawn on POD 297 prior to the 1-year visit.

Conclusion

At 1-year in the COMPASSION S3 PAS, we report:

- High rate of device success
- No deaths and low rates of THV dysfunction, reintervention, and endocarditis
- Sustained improvement in valve performance, with:
 - >99% of patients demonstrating none, trace, or mild PR
 - Reduced and stable RVOT mean gradients

Continued follow-up through 5 years will further inform long-term valve performance and clinical outcomes

Thanks and Recognition

Participating Sites

Duke University Medical Center, NC – *Gregory Fleming*

Mount Sinai Hospital, NY – *Barry Love*

Children's Hospital Colorado, CO – *Jenny Zablah*

Boston Children's Hospital, MA – *Nicola Maschietto*

Advocate Children's Hospital, IL – *Alexander Javois*

Children's Health Dallas, TX – *Thomas Zellers*

University of Virginia, VA – *Michael Hainstock*

Children's Hospital of Philadelphia, PA – *Matthew Gillespie*

Minneapolis Heart Institute Foundation, MN – *Victor Cheng*

Dell Children's Medical Center, TX – *D. Byron Holt*

Cedars-Sinai, CA – *Stephen Nageotte*

University of Alabama at Birmingham, AL – *Mark A. Law*

University of Utah at Primary Children's Hospital, UT – *Robert Gray*

Cincinnati Children's Hospital, OH – *Shabana Shahanavaz*

Participating Sites

Columbia University Irving Medical Center, NY – *Alejandro Torres*

Nationwide Children's Hospital, OH – *Arash Salavitabar*

UPMC Children's Hospital of Pittsburgh, PA – *Jacqueline Kreutzer*

Newark Beth Israel Medical Center, NJ – *Marc Cohen*

St. Louis Children's Hospital, MO – *David Balzer*

Clinical Events Committee

Cardiovascular Research Foundation, NY

Echocardiographic Core Laboratory

Children's Mercy, Kansas City, MO

Directors: *Girish Shirali, Anitha Parthiban*

Sponsor

Edwards Lifesciences, Irvine, CA

Important Safety Information

Edwards SAPIEN 3 Transcatheter Heart Valve System – Pulmonic

Indications: The Edwards SAPIEN 3 Transcatheter Heart Valve (THV) System with Edwards SAPIEN 3 Transcatheter Pulmonic Valve Delivery System (or Edwards Commander Delivery System) is indicated for use in the management of pediatric and adult patients who have a clinical indication for intervention on a dysfunctional right ventricular outflow tract (RVOT) conduit or surgical bioprosthetic valve in the pulmonic position with $\geq$ moderate regurgitation and/or a mean RVOT gradient of $\geq$ 35 mmHg.

Contraindications: The Edwards SAPIEN 3 THV System with Edwards SAPIEN 3 Transcatheter Pulmonic Valve Delivery System (or Edwards Commander Delivery System) is contraindicated in patients who cannot tolerate an anticoagulation/antiplatelet regimen or who have active bacterial endocarditis or other active infections.

Warnings: The devices are designed, intended, and distributed for single use only. **Do not resterilize or reuse the devices.** There are no data to support the sterility, nonpyrogenicity, and functionality of the devices after reprocessing. Correct sizing of the valve into the non-compliant RVOT conduit or failing bioprosthesis (landing zone) is essential to minimize risks. Too small of a valve may result in paravalvular leak, migration, or valve embolization; whereas too large of a valve may result in residual gradient (patient-prosthesis mismatch) or RVOT rupture. Accelerated deterioration of the valve may occur in patients with an altered calcium metabolism. Assessment for coronary compression risk prior to valve implantation is essential to prevent the risk of severe patient harm. The physician must verify correct orientation of the valve prior to its implantation; the inflow (outer skirt end) of the valve should be oriented towards the proximal end (handle) of the delivery system to prevent the risk of severe patient harm. Prior to delivery, the valve must remain hydrated at all times and cannot be exposed to solutions other than its shipping storage solution and sterile physiologic rinsing solution. Valve leaflets mishandled or damaged during any part of the procedure will require replacement of the valve. Patients with pre-existing bioprostheses should be carefully assessed prior to implantation of the valve to ensure proper valve positioning and deployment. Do not use the valve if the tamper evident seal is broken, the storage solution does not completely cover the valve, the temperature indicator has been activated, the valve is damaged, or the expiration date has elapsed. Do not mishandle the delivery system or use it if the packaging or any components are not sterile, have been opened or are damaged (e.g. kinked or stretched), or the expiration date has elapsed. Use of excessive contrast media may lead to renal failure. Measure the patient's creatinine level prior to the procedure. Contrast media usage should be monitored. Patient injury could occur if the Commander delivery system is not un-flexed prior to removal. Care should be exercised in patients with hypersensitivities to cobalt, nickel, chromium, molybdenum, titanium, manganese, silicon, and/or polymeric materials. The procedure should be conducted under fluoroscopic guidance. Some fluoroscopically guided procedures are associated with a risk of radiation injury to the skin. These injuries may be painful, disfiguring, and long-lasting. It is recommended that all prosthetic heart valve recipients be prophylactically treated for endocarditis to minimize the possibility of prosthetic valve infection. Valve recipients should be maintained on anticoagulant/antiplatelet therapy, except when contraindicated, as determined by their physician. This device has not been tested for use without anticoagulation. Do not add or apply antibiotics to the storage solution, rinse solutions or to the valve.

Precautions: Long-term durability has not been established for the valve. Regular medical follow-up is advised to evaluate valve performance. Glutaraldehyde may cause irritation of the skin, eyes, nose and throat. Avoid prolonged or repeated exposure to, or breathing of, the solution. Use only with adequate ventilation. If skin contact occurs, immediately flush the affected area with water; in the event of contact with eyes, seek immediate medical attention. For more information about glutaraldehyde exposure, refer to the Material Safety Data Sheet available from Edwards Lifesciences. To maintain proper valve leaflet coaptation, do not overinflate the deployment balloon. Appropriate antibiotic prophylaxis is recommended post-procedure in patients at risk for prosthetic valve infection and endocarditis. Patient venous anatomy should be evaluated to prevent the risk of access that would preclude the delivery and deployment of the device. Patient should be heparinized to maintain the ACT at $\geq$ 250 sec prior to introduction of the delivery system in order to prevent thrombosis. Safety and effectiveness have not been established for patients with the following characteristics/comorbidities: Blood dyscrasias defined as: leukopenia, acute anemia, thrombocytopenia, or history of bleeding diathesis or coagulopathy. A known hypersensitivity or contraindication to aspirin, heparin, ticlopidine (Ticlid™), or clopidogrel (Plavix™), or sensitivity to contrast media, which cannot be adequately premedicated. Positive urine or serum pregnancy test in female subjects of child-bearing potential. Residual mean gradient may be higher in a "THV-in-failing bioprosthesis" configuration than that observed following implantation of the valve inside a native annulus using the same size device. Patients with elevated mean gradient post procedure should be carefully followed. It is important that the manufacturer, model and size of the preexisting bioprosthetic valve be determined, so that the appropriate valve can be implanted and a prosthesis-patient mismatch be avoided. Additionally, pre-procedure imaging modalities must be employed to make as accurate a determination of the inner diameter as possible.

Potential Adverse Events: Potential risks associated with the anesthesia, interventional procedure and imaging include but are not limited to: death; stroke/transient ischemic attack; respiratory insufficiency or respiratory failure; cardiovascular or vascular injury, such as perforation or damage (dissection) of vessels, myocardium or valvular structures including rupture of the RVOT that may require intervention; pericardial effusion/cardiac tamponade; embolic event: air, calcific material, thrombus, device fragments; infection including incisional site infection, septicemia and endocarditis; myocardial infarction; renal insufficiency or renal failure; conduction system injury, arrhythmia, arteriovenous (AV) fistula; systemic or peripheral nerve injury, systemic or peripheral ischemia, pulmonary edema, pneumothorax, pleural effusion, atelectasis; blood loss requiring transfusion; anemia; radiation injury; electrolyte imbalance; hypertension or hypotension; allergic reaction to anesthesia, contrast media, antithrombotic therapy, device materials; hematoma or ecchymosis, syncope, pain, exercise intolerance or weakness, inflammation; angina; fever; cardiac failure. Potential risks associated with the valve, delivery system and/or accessories include, but may not be limited to, the following: cardiac arrest; cardiogenic shock; coronary flow obstruction/transvalvular flow disturbance, device thrombosis requiring intervention; injury to tricuspid valve; device embolization requiring intervention; device acute migration or malposition requiring intervention; endocarditis; hemolysis / hemolytic anemia; THV dysfunction resulting in pulmonary valve symptoms; mechanical failure of delivery system, and/or accessories; emergent and non-emergent re-intervention; dyspnea.

Important Safety Information (continued)

Edwards Crimper

Indications: The Edwards crimper is indicated for use in preparing the Edwards SAPIEN 3 transcatheter heart valve for implantation.

Contraindications: There are no known contraindications.

Warnings: The device is designed, intended, and distributed for single use only. **Do not resterilize or reuse the device.** There are no data to support the sterility, nonpyrogenicity, and functionality of the device after reprocessing. Do not mishandle the device. Do not use the device if the packaging or any components are not sterile, have been opened or are damaged, or the expiration date has elapsed.

Precautions: For special considerations associated with the use of the Edwards crimper prior to THV implantation, refer to the THV Instructions for Use.

Potential Adverse Events: There are no known potential adverse events associated with the Edwards crimper.

CAUTION: Federal (United States) law restricts these devices to sale by or on the order of a physician.

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