# Primary Results From the Evolut Low Risk Bicuspid Study

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For the Evolut Low Risk Bicuspid Investigators

# Disclosure Statement of Financial Interests



Within the past 12 months, I have had a financial interest/arrangement or affiliation with the organization(s) listed below.

| Financial Relationship | Company |
| --- | --- |
| Research grants, consulting fees | AtriCure, Liva Nova, Medtronic |

Medtronic personnel performed all statistical analyses and assisted with the graphical display of the data presented.

# Background



- TAVR with Evolut supra-annular self-expanding valves has demonstrated excellent outcomes in tricuspid aortic stenosis and is currently approved in the US for patients across all risk classes.

- Patients with bicuspid aortic stenosis have been generally excluded from prior TAVR trials, due to concerns of:
  - Asymmetric calcification, elliptical shape, potential incomplete valve expansion, procedural technical concerns etc.
  - Annular vs. supra-annular measurements

- There have been no prospective studies assessing TAVR in low risk patients with bicuspid aortic stenosis.

# Objective



To assess the safety and efficacy of TAVR in patients with bicuspid aortic valve stenosis and low surgical risk

# Participating Sites

Evolut™ Low Risk Bicuspid Study

# Study Administration



**Principal Investigators:** John Forrest, Basel Ramlawi

**Executive Committee:** John Forrest, Jeffrey Popma, Basel Ramlawi, Michael Reardon

**Screening Committee:** G. Michael Deeb (Chair), John Forrest, Jeffrey Popma, Basel Ramlawi, Michael Reardon, Steven Yakubov

**Echo Core Laboratory:** Jae Oh, Mayo Clinic, Rochester, MN

**Data & Safety Monitoring Board:** David Faxon (Chair), William Holman, John Lopez, Scott Kasner, John Orav

**Clinical Events Committee:** Cliff Berger, Scott Bortman, Manish Chauhan, Donald Cutlip, Torin Fitton, Eli Gelfand, David Grossman, Claudia Hochberg (Chair), Carey Kimmelstiel, Daniel Kramer, Megan Leary, Robert Rodriguez, Sanjay Samy, Jonathan Silver, Gregory Smaroff, David Thaler, Jonathan Waks, Sergio Waxman, David Weiss, Jeffrey Veluz

**Sponsor:** Medtronic, Minneapolis, MN

# Study Methods

Evolut™ Low Risk Bicuspid Study

- Multicenter, prospective, interventional, single-arm study
- Baseline MSCT to confirm bicuspid morphology
- Patient eligibility reviewed by local Heart Team & Screening Committee
- Implant Procedure
  - Annular sizing recommended for all patients
  - Pre-TAVR balloon valvuloplasty strongly encouraged
- CEC adjudicated all endpoint-related adverse events
- Hemodynamics centrally assessed by echocardiographic core laboratory
- Patient follow-up planned for 10 years

# Valves Studied



| Evolut R Valve [43%] | Evolut PRO Valve [57%] |
|---|---|
| 23, 26, 29 and 34 mm | 23, 26 and 29 mm |

# Key Inclusion Criteria



- Bicuspid aortic valve anatomy confirmed by MSCT
- Symptomatic and asymptomatic severe AS[1]
- A predicted risk of 30-day mortality <3% per multidisciplinary local Heart Team assessment

[1]Nishimura RA, et al. Circulation. 2014;129:2440-92.

# Key Exclusion Criteria

Evolut™ Low Risk Bicuspid Study

- Age < 60 years
- Multivessel coronary artery disease (SYNTAX score >22)
- Ascending aorta diameter > 4.5 cm
- Aortopathy requiring surgical intervention
- Prohibitive LVOT calcification
- Anatomic dimensions outside recommended range
  - SOV (≥ 25 mm)
  - Annulus (18 to 30 mm)
  - Trileaflet aortic valve on MSCT

# Study Endpoints



## Primary Safety Endpoint

All-cause mortality or disabling stroke at 30 days

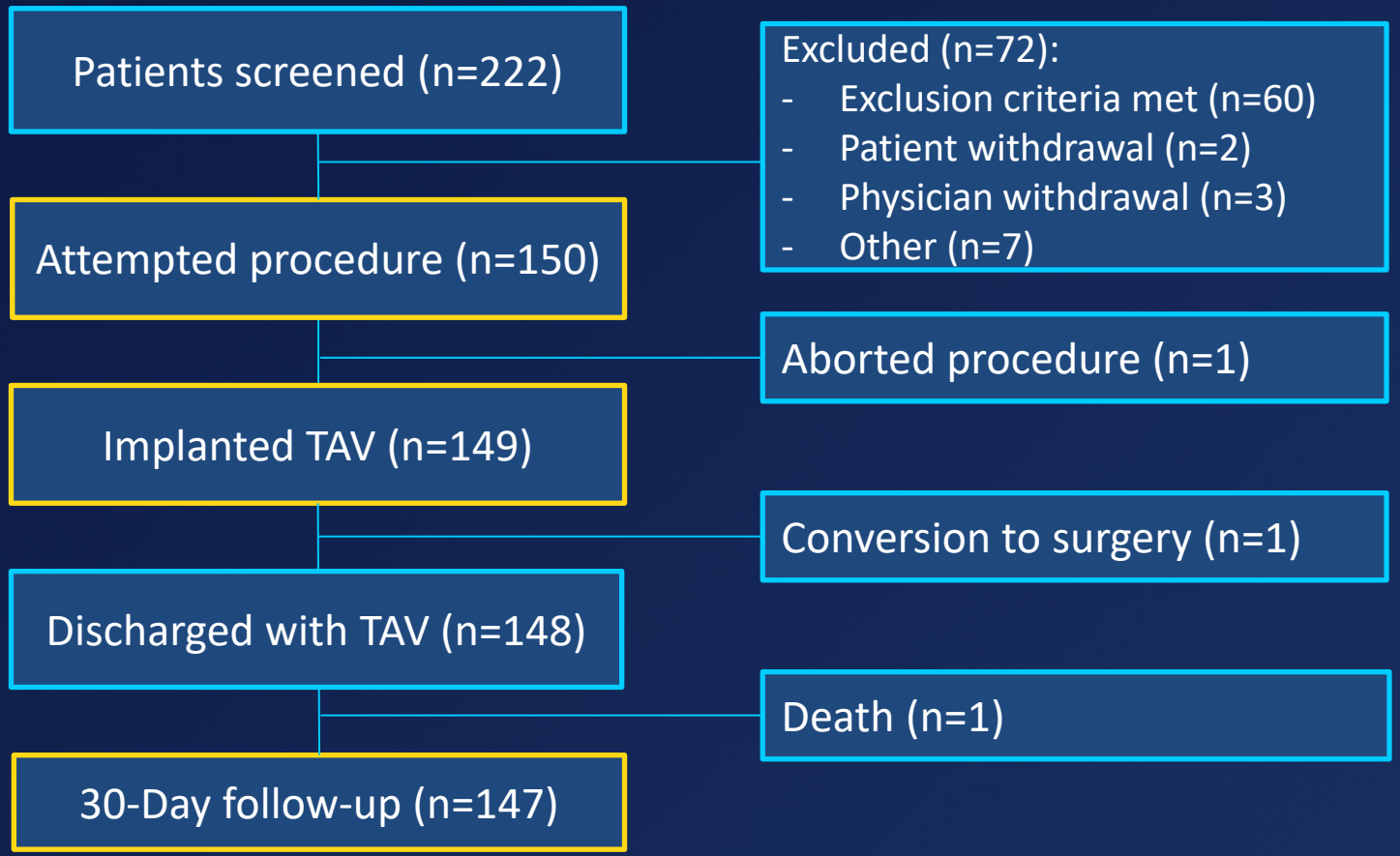
## Primary Efficacy Endpoint

Device Success

- Absence of procedural mortality AND
- Correct position of 1 valve in the proper anatomical location AND
- Absence of > mild aortic valve regurgitation

# Patient Flow





# Reasons for Study Exclusion



| Reason | N = 60 |
|---|---|
| Anatomical reasons | 46 |
| Tricuspid aortic valve | 17 |
| Aortic root dimensions: annular perimeter/diameter | 15 |
| Mean ascending aorta > 45 mm | 9 |
| Aortic root dimensions: SOV diameter | 4 |
| Prohibitive LVOT calcification | 1 |
| Risk of mortality outside protocol (> low risk) | 5 |
| Contraindication for placement of bioprosthetic valve | 3 |
| Allergies | 2 |
| Did not meet severe AS criteria | 2 |
| Age less than 60 years | 1 |
| Other condition excluding from study per investigator | 1 |

# RESULTS

# Baseline Clinical Characteristics



| Mean ± SD or no. (%) | N = 150 |
|---|---|
| Age, years | 70.3 ± 5.5 |
| Male sex | 78 (52.0) |
| Body surface area, $m^2$ | 1.9 ± 0.2 |
| STS PROM, % | 1.4 ± 0.6 |
| NYHA Class III or IV | 41 (27.3) |
| Peripheral arterial disease | 14 (9.3) |
| Chronic lung disease/ COPD | 26 (17.7) |
| Prior coronary artery bypass grafting | 2 (1.3) |
| Mean gradient, mm Hg | 48.0 ± 16.1 |
| Aortic valve area, $cm^2$ | 0.8 ± 0.2 |

# Bicuspid Valve Sievers Subtypes

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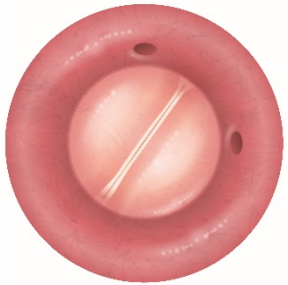
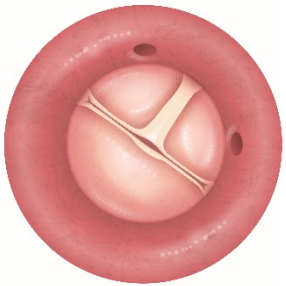
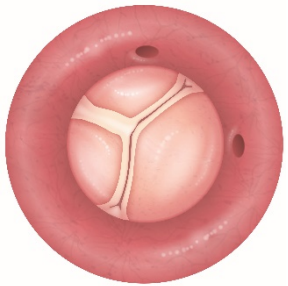
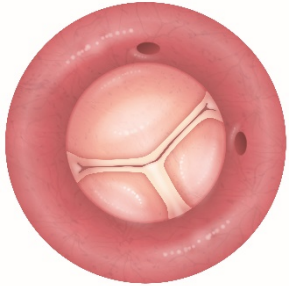
| Type 0<br>N = 14 | Type I<br>Left-Right<br>N = 107 | Type I<br>Right-Non<br>N=27 | Type I<br>Non-Left<br>N= 2 |
|---|---|---|---|
|  |  |  |  |
| 9.3% | 71.3% | 18.0% | 1.3% |

No patients had Sievers Type 2.

# Procedural Characteristics

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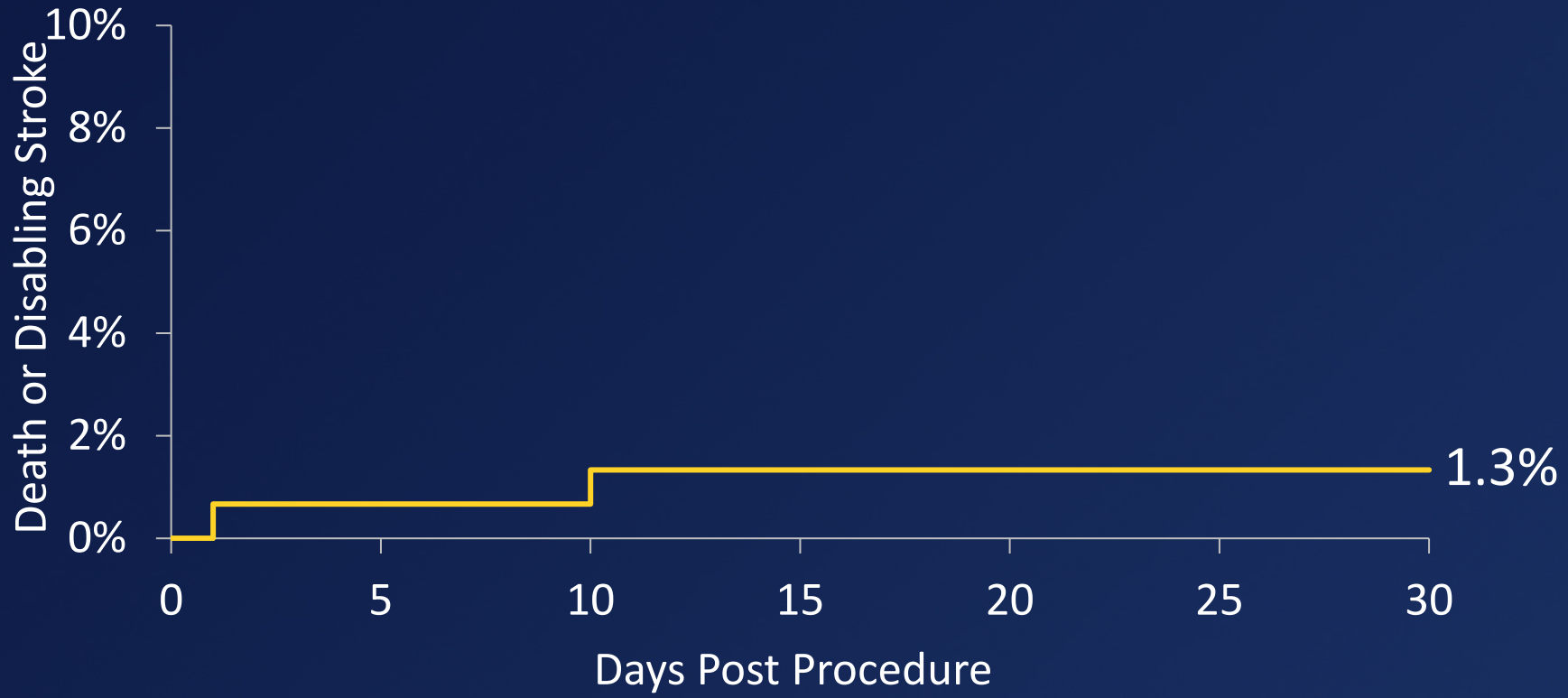
| No. (%) | N = 149* |
|---|---|
| General anesthesia | 95 (63.3) |
| Iliofemoral access | 147 (98.7) |
| Embolic protection | 45 (30.0) |
| Pre-TAVR balloon dilation | 137 (91.3) |
| Post-TAVR balloon dilation | 55 (36.9) |
| > 1 valve implanted | 5 (3.3) |

| No. (%) | N = 149* |
|---|---|
| Resheath or recapture | 49 (32.9) |
| Implanted valve size | |
| 23 mm | 0 (0.0) |
| 26 mm | 32 (22.4) |
| 29 mm | 55 (36.9) |
| 34 mm§ | 62 (41.6) |

*For 1 patient, the procedure was aborted. §Only Evolut R

# Primary Endpoint






| | | |
|---|---|---|
| No. at Risk | 150 | 143 |

# Outcomes at 30 Days



| No. of patients (KM estimates as %) | N = 150 |
|---|---|
| All-cause mortality or disabling stroke | 2 (1.3) |
| All-cause mortality | 1 (0.7) |
| Disabling stroke | 1 (0.7) |
| Non-disabling stroke | 5 (3.3) |
| Major vascular complication | 2 (1.3) |
| Aortic dissection | 0 (0.0) |
| Annular rupture | 0 (0.0) |
| Permanent pacemaker* | 22 (14.7) |
| Permanent pacemaker† | 22 (15.1) |
| Coronary artery obstruction | 1 (0.7) |

*Includes patients with baseline permanent pacemaker. †Excludes patients with baseline permanent pacemaker.

# Additional Outcomes at 30 Days



| No. of patients (%) | |
|---|---|
| Device success | 141/148 (95.3) |
| Patient-prosthesis mismatch* | |
| None | 115 (87.1) |
| Moderate | 10 (7.6) |
| Severe | 7 (5.3) |
| Mean gradient > 20 mm Hg | 2/146 (1.4) |

*N=132 patients per VARC-2.

# Valve Hemodynamics

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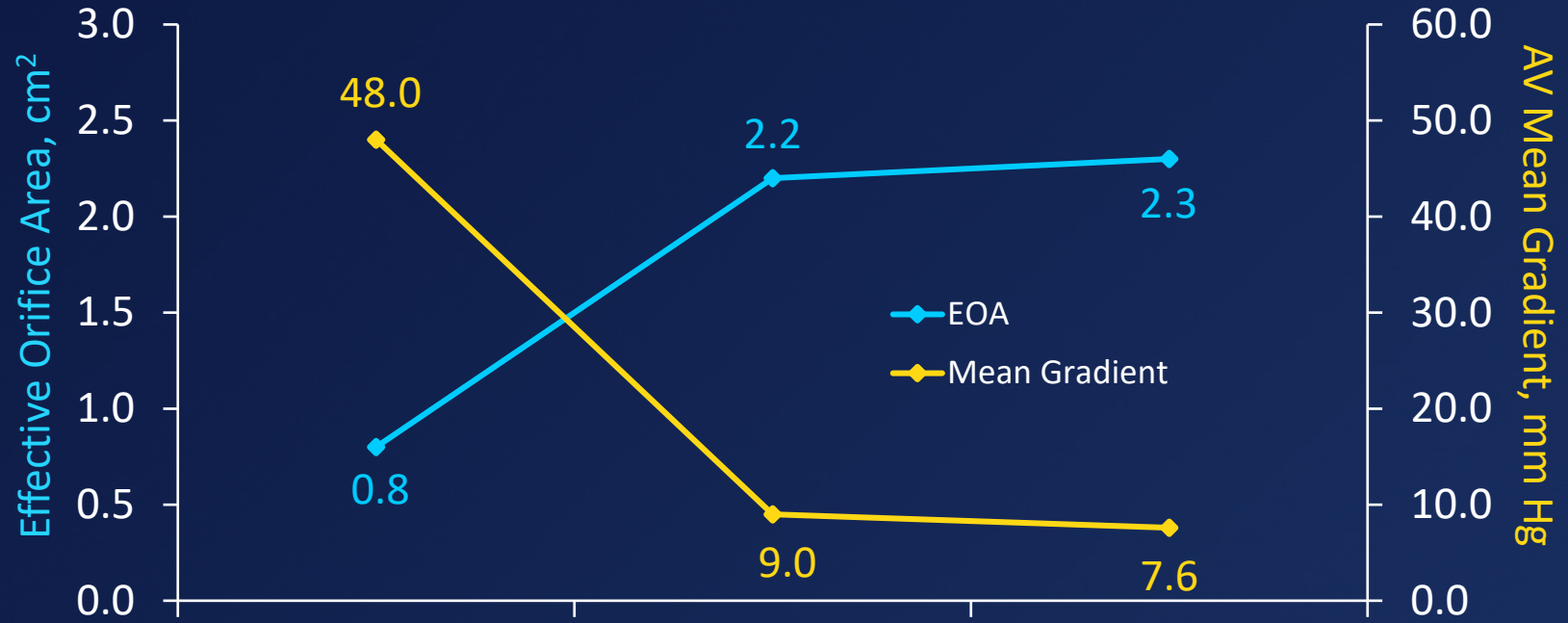
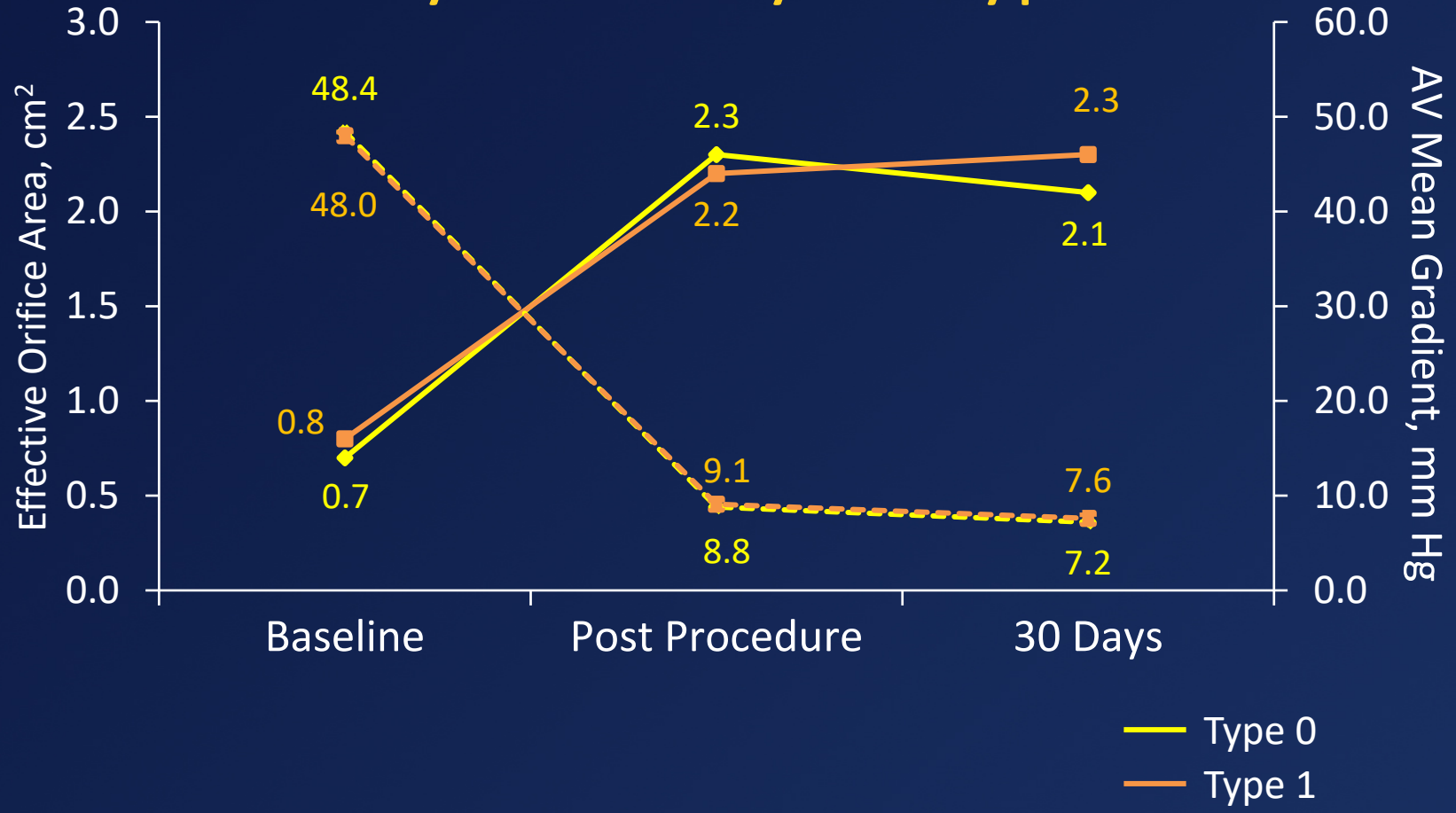



| No. of Echos | Baseline | Post Procedure | 30 Days |
|---|---|---|---|
| EOA | 135 | 124 | 132 |
| AVG | 148 | 146 | 146 |

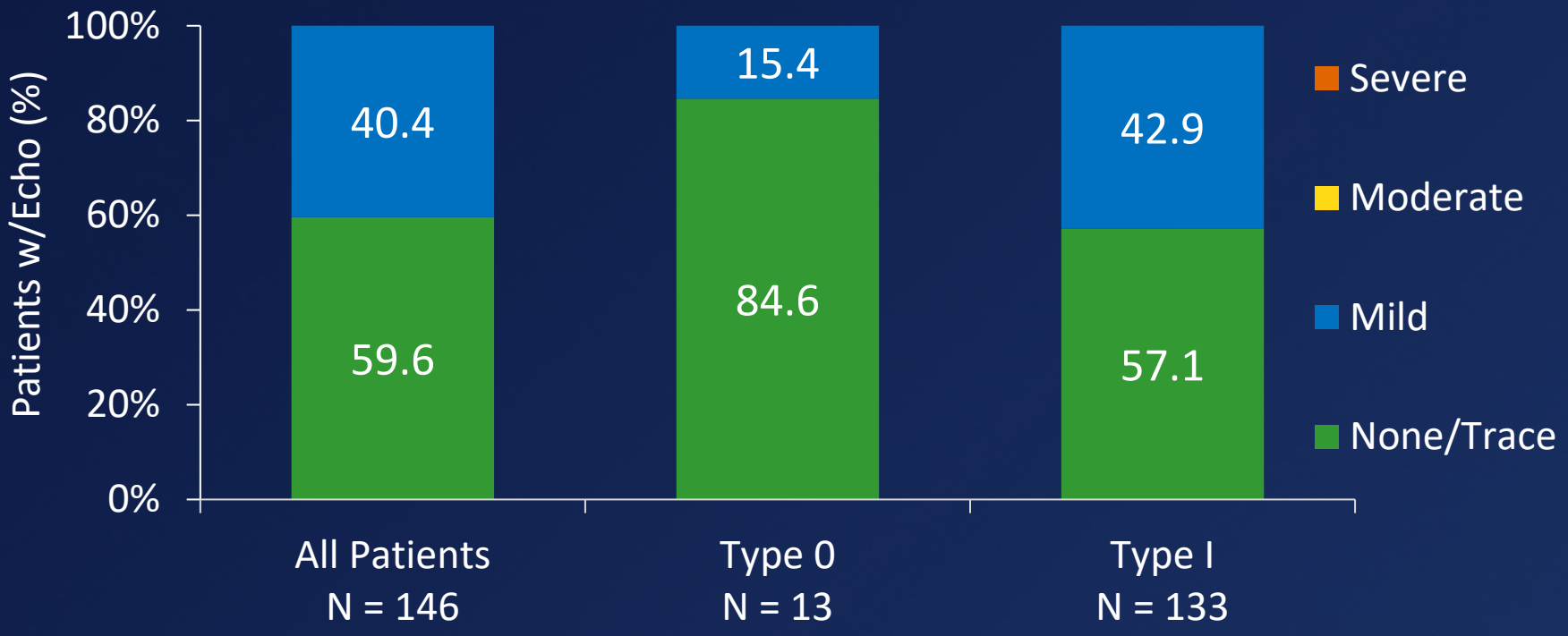
# Valve Hemodynamics by Subtypes

Evolut™ Low Risk Bicuspid Study



# Total Aortic Valve Regurgitation






Implant population. Core lab assessments.

# New York Heart Association

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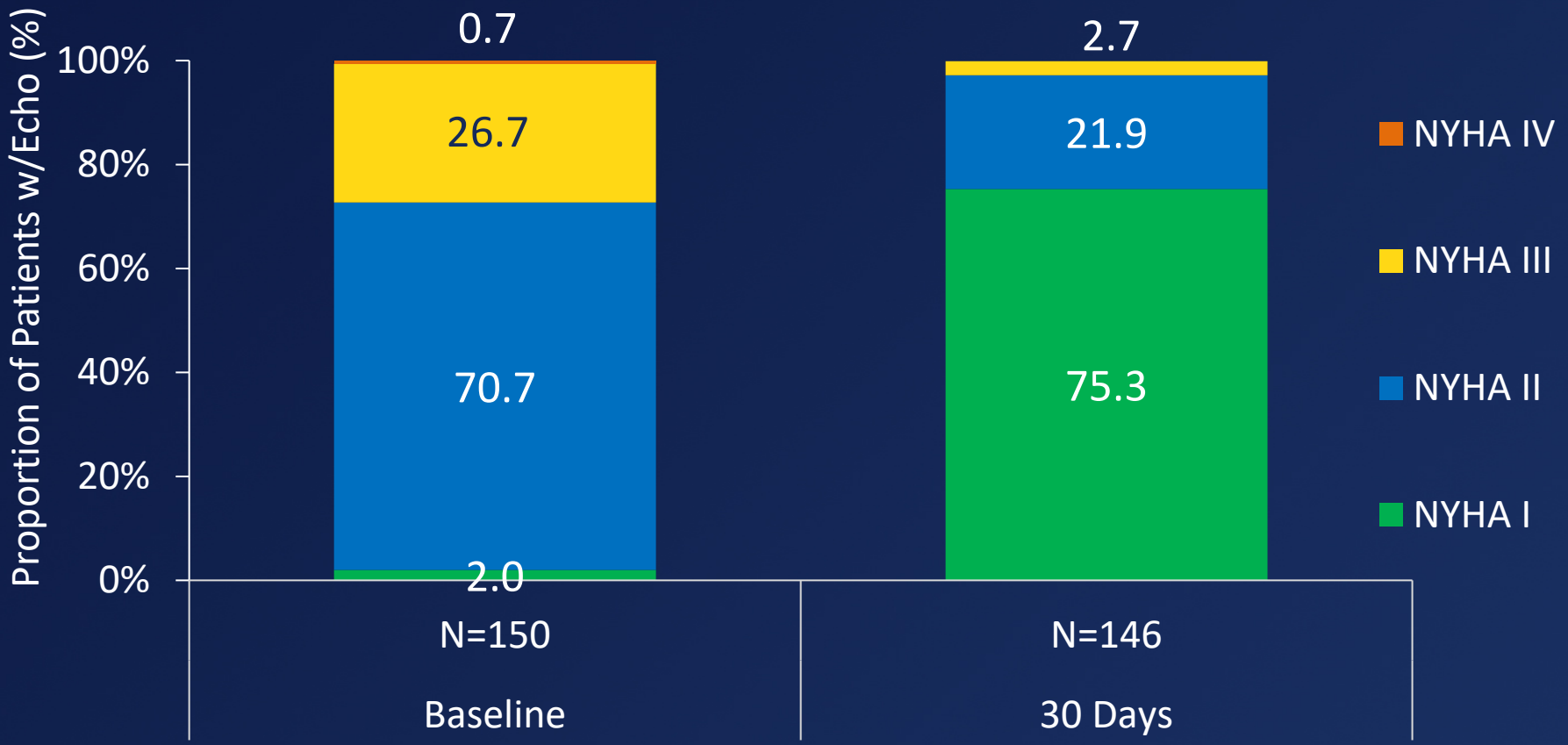

# Discussion



- Study performed at high volume expert centers
- Non-randomized study design
- Standardized implant technique
  - Annular sizing
  - Pre-TAVR balloon dilation
- Rigorous adherence to patient selection parameters

# Summary



- TAVR with Evolut supra-annular self-expanding valve in low-risk bicuspid patients achieved excellent early results:
  - Annular sizing achieved 95.3% device success
  - Low mortality and stroke at 30 days (1.3%)
  - Low rates of PVL (no moderate/severe)
  - Consistent hemodynamics across Sievers Classification
- Patients will be followed for 10 years

# Clinical Implications

Evolut™ Low Risk Bicuspid Study

- In low-risk AS patients with bicuspid morphology, TAVR with Evolut can be considered a viable alternative to SAVR… after considering anatomic, clinical and patient social factors.

- Data is based on short-term results and needs to be confirmed long-term in this low-risk cohort.