CoreValve for High Risk and Extreme Risk Patients; The US Pivotal Trials

X CONGRESO COLEGIO COLOMBIANO
DE HEMODINAMIA E INTERVENCIONISMO CARDIOVASCULAR
XXIV JORNADAS SOLACI - 8VAS. REGIÓN ANDINA

COLEGIO COLOMBIANO DE HEMODINAMIA E INTERVENCIONISMO CARDIOVASCULAR

SOLACI SOCIEDAD LATINOAMERICANA DE CARDIOLOGIA INTERVENCIONISTA

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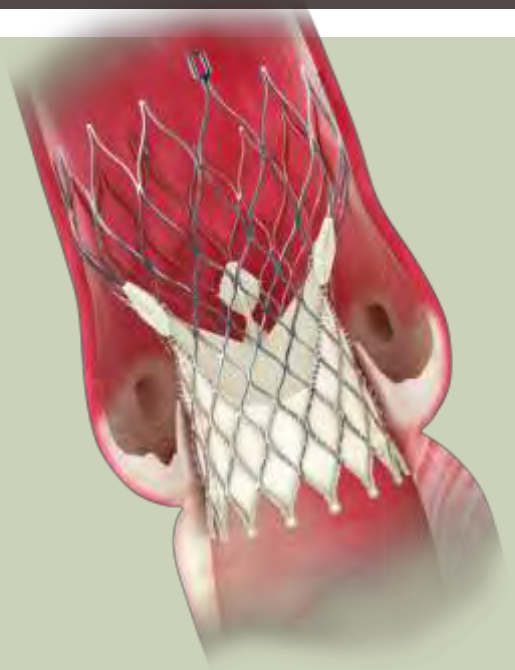
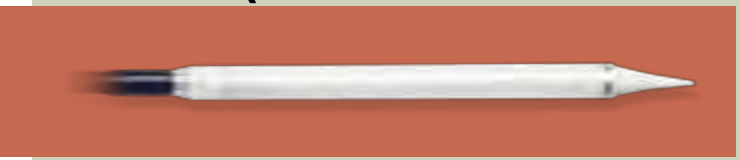
Angiografia de Occidente S.A.
Somos todo corazón

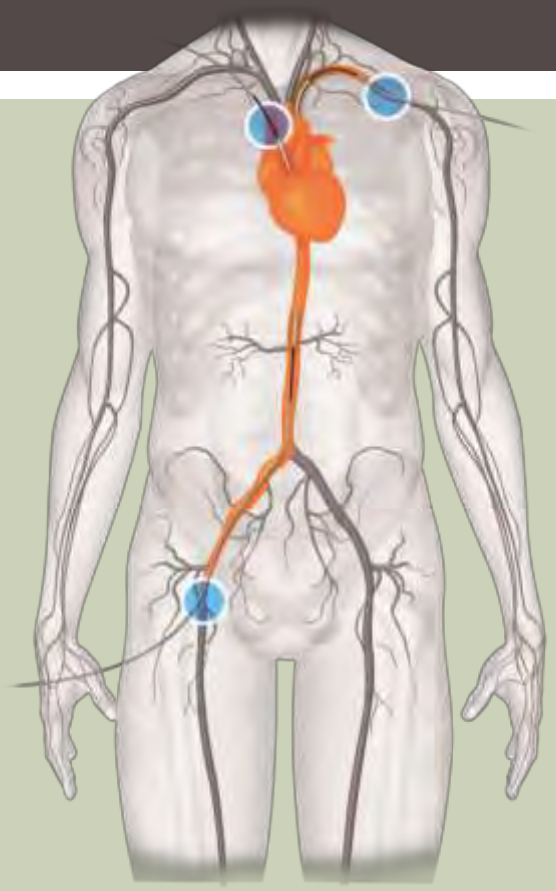
Study Device and Access Routes



4 valve sizes
(18-29 mm annular range)



18Fr delivery system



Transfemoral
Subclavian
Direct Aortic

2007- 2010

First CoreValve Transcatheter AVR by Retrograde Approach
Laborde, Lal, Grube – July 12, 2004

First CoreValve PERCUTANEOUS AVR by Retrograde Approach – Oct 12, 2006
Serruys, DeJaegere, Laborde

First CoreValve AVR by Trans-aortic Approach – Nov.., 2008
Lange, Baumschmitt, Bleizzifer

First CoreValve AVR by Axillary Approach – June 30, 2006
Serruys, DeJaegere, Laborde

First CoreValve AVR by Transapical Approach – Jul 19, 2007
Lange, Bauernschmitt, Laborde

First CoreValve AVR by Carotid Approach – Oct 19, 2009
Modine, Sudre

US Pivotal trial
Popma J. PI

2004 2005 2006 2007 2008 2009 2010 …2013

G 1
12 July 2004

G 2
15 Sept 2005

G 3
22 Sept 2006

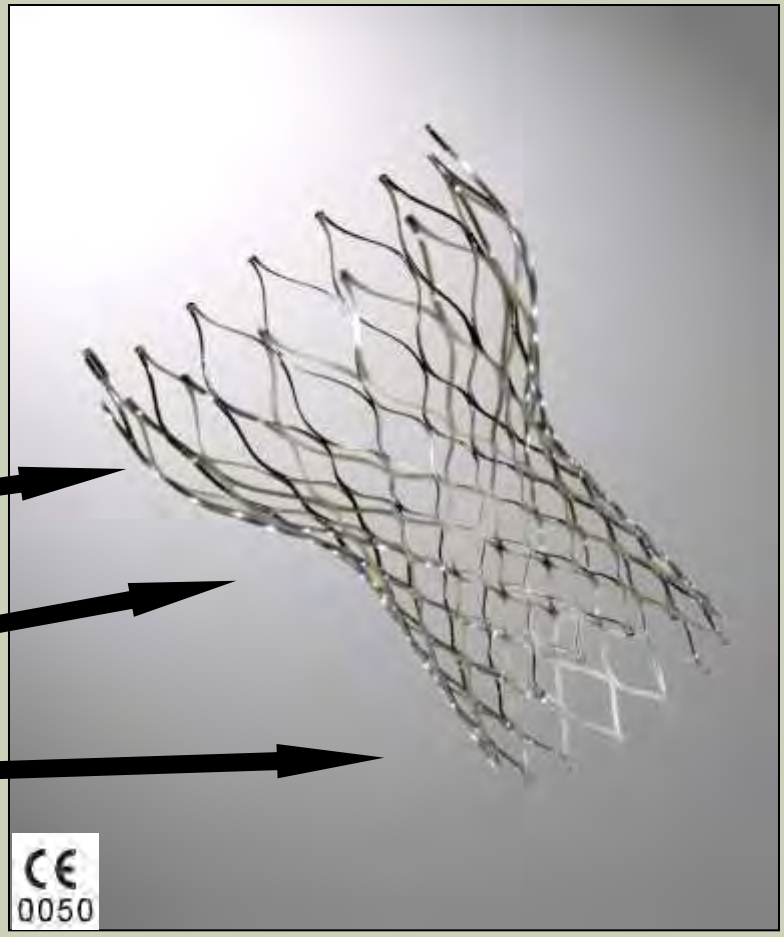
CE Mark

US Pivotal trial

FDA
Approval

Modified Laborde, J C.

Self-Expanding Multi-level Support Frame



Diamond cell configuration

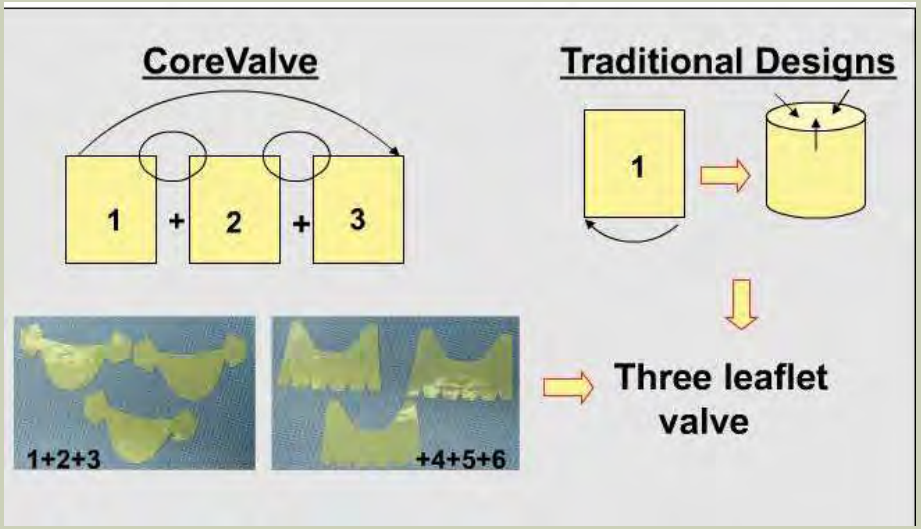
Nitinol: memory shaped/no recoil Multi-level design incorporates three *different* areas of radial and hoop strength

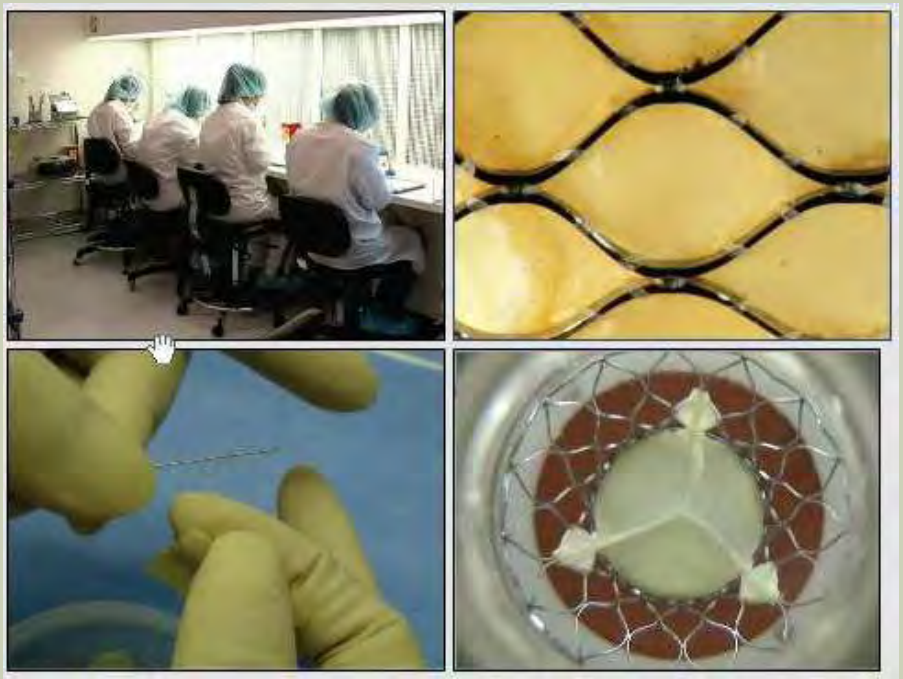
Low radial force area orients the system

Constrained area avoids coronaries and features supra-annular valve leaflets

- **High radial force provides secure anchoring and constant force mitigates paravalvular leak**

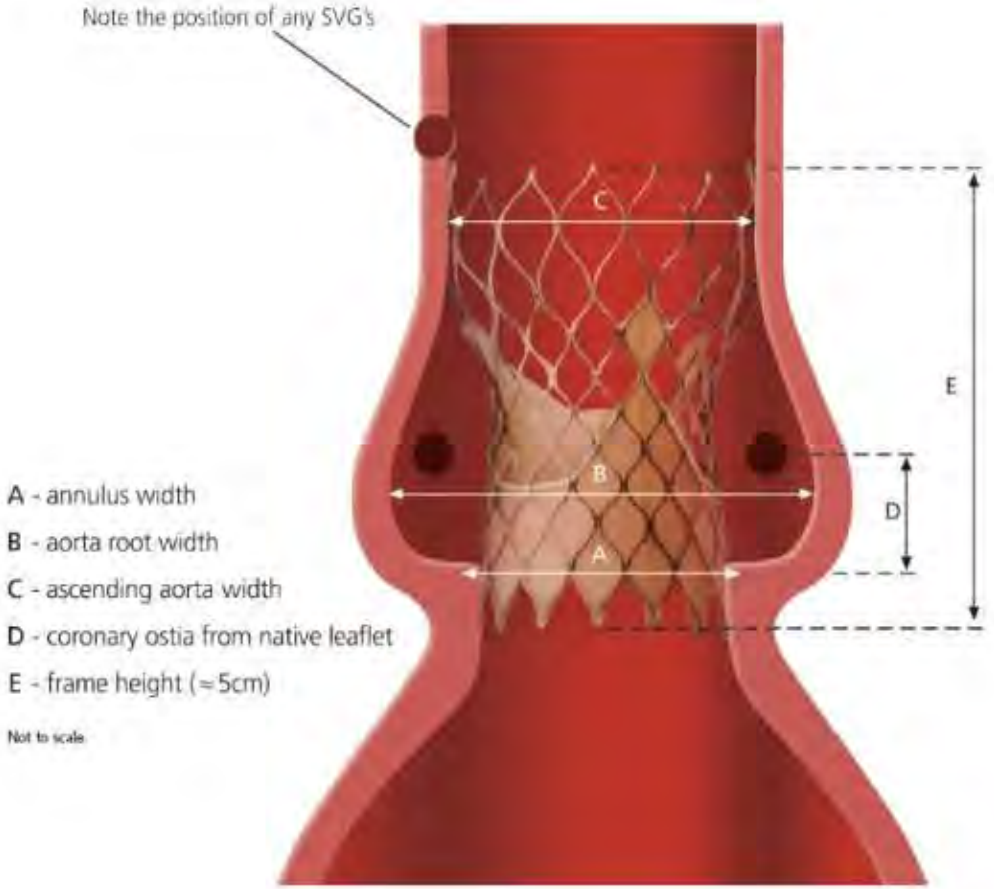
Radiopaque


CoreValve
Traditional Designs
1
+
2
+
3
1
1+2+3
+4+5+6
Three leaflet valve



Porcine Pericardial Tissue Valve

- *Specifically designed for transcatheter delivery*
- **Single layer porcine pericardium**
- **Tri-leaflet configuration**
- **Tissue valve sutured to frame**
- **Standard tissue fixation techniques**
- **200M cycle AWT testing completed**
- *Supra-annular valve function*
- *Intra-annular implantation and sealing skirt*



A - annulus width

B - aorta root width

C - ascending aorta width

D - coronary ostia from native leaflet

E - frame height (≈5cm)

Not to scale

CoreValve
THE REVALVING TECHNOLOGY

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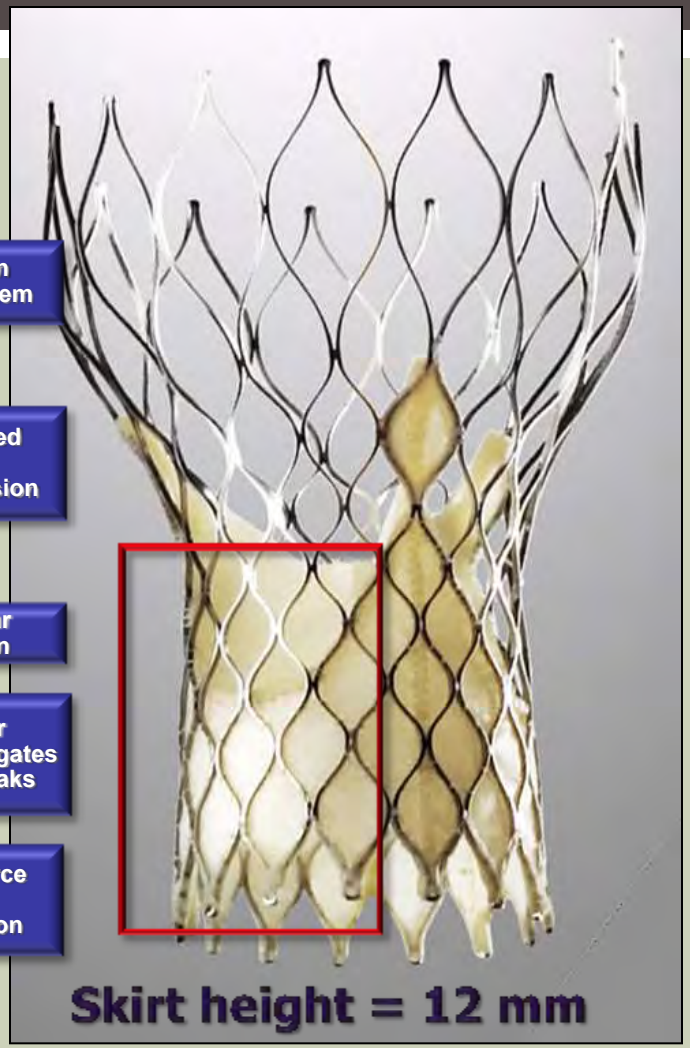
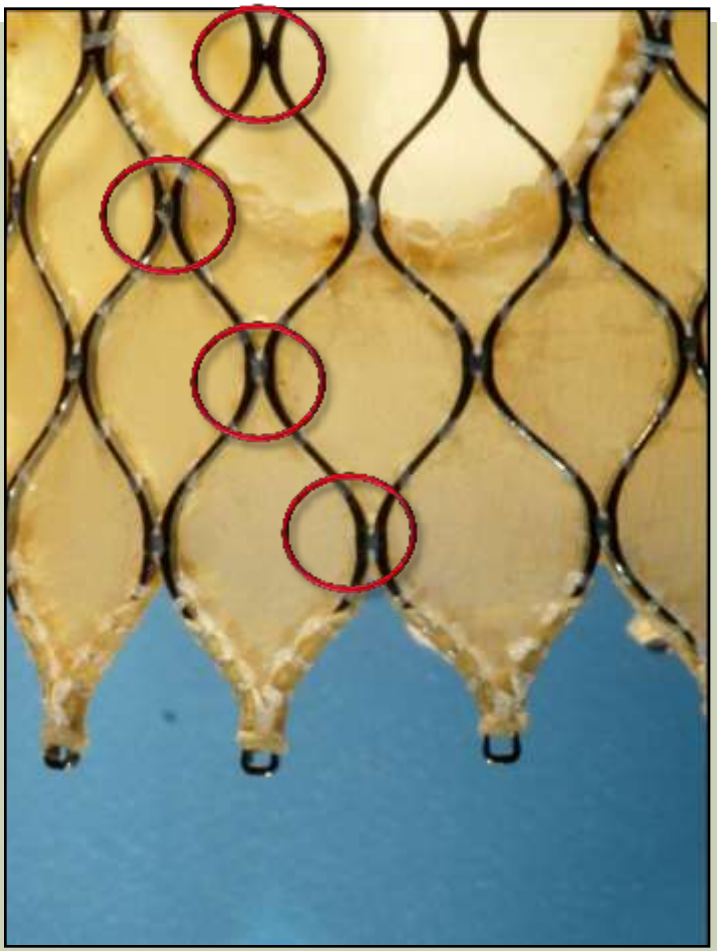
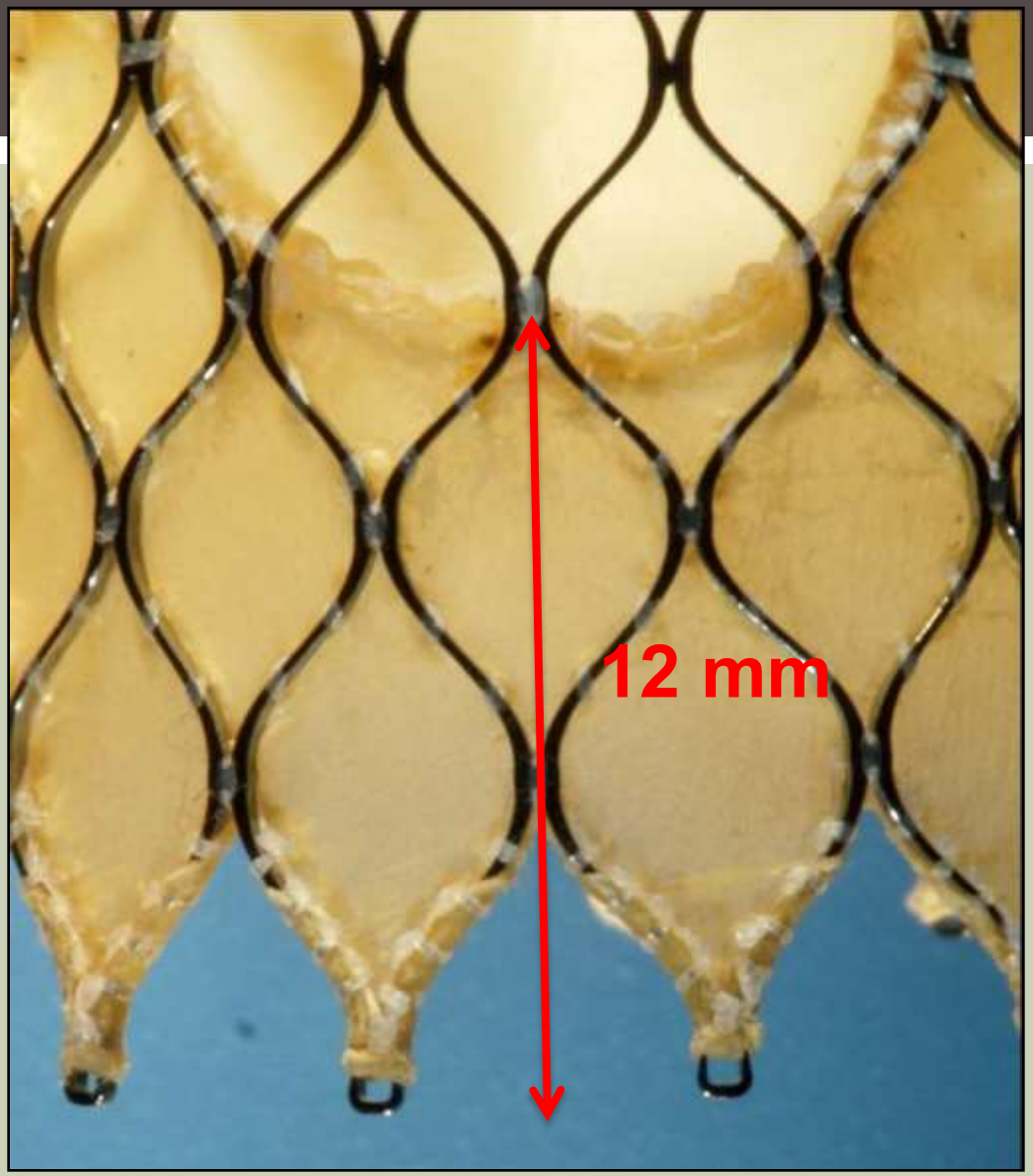
COREVALVE BIOPROSTHESIS





LANDING ZONE



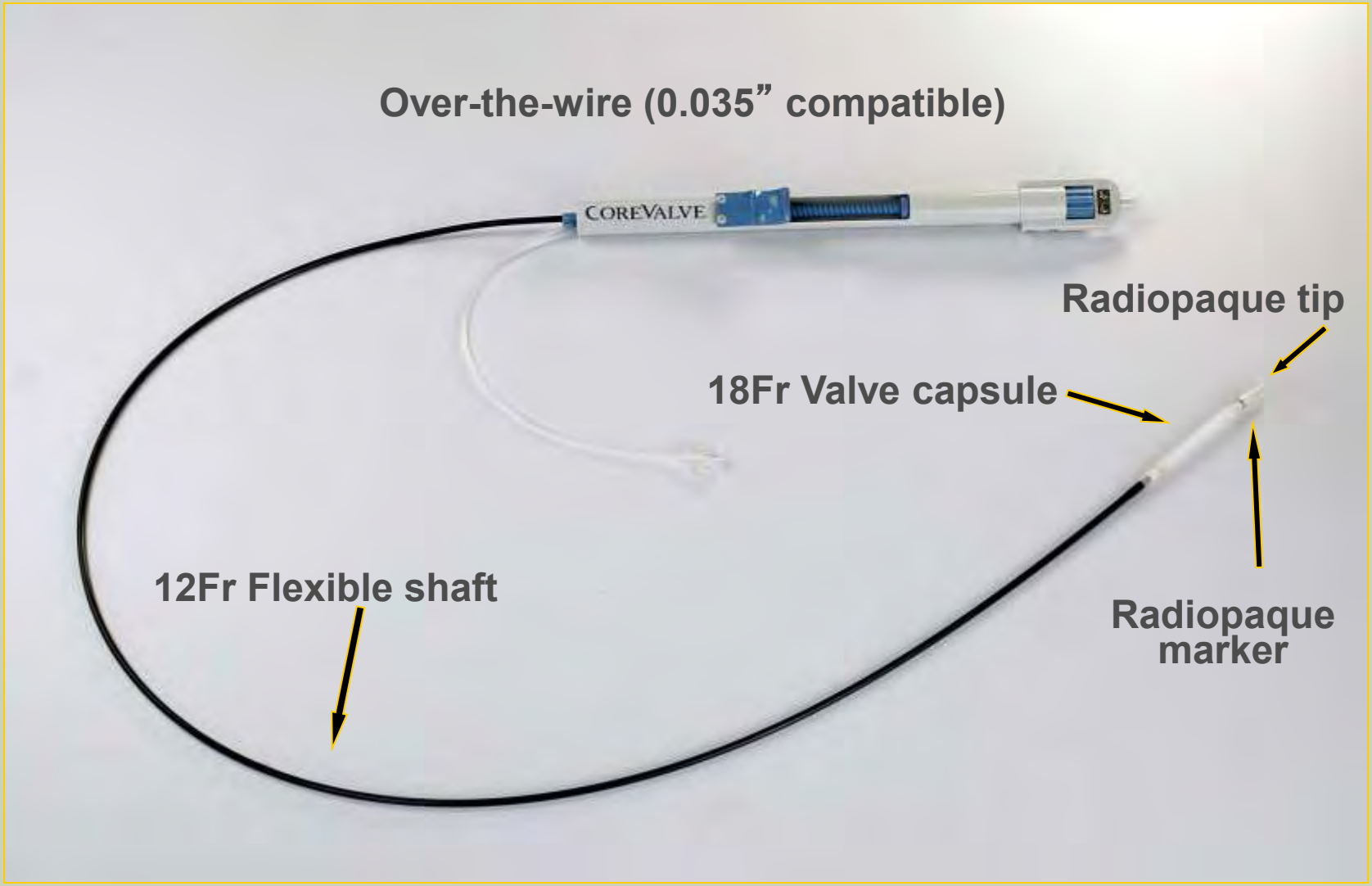
COREVALVE

VALVE SIZE

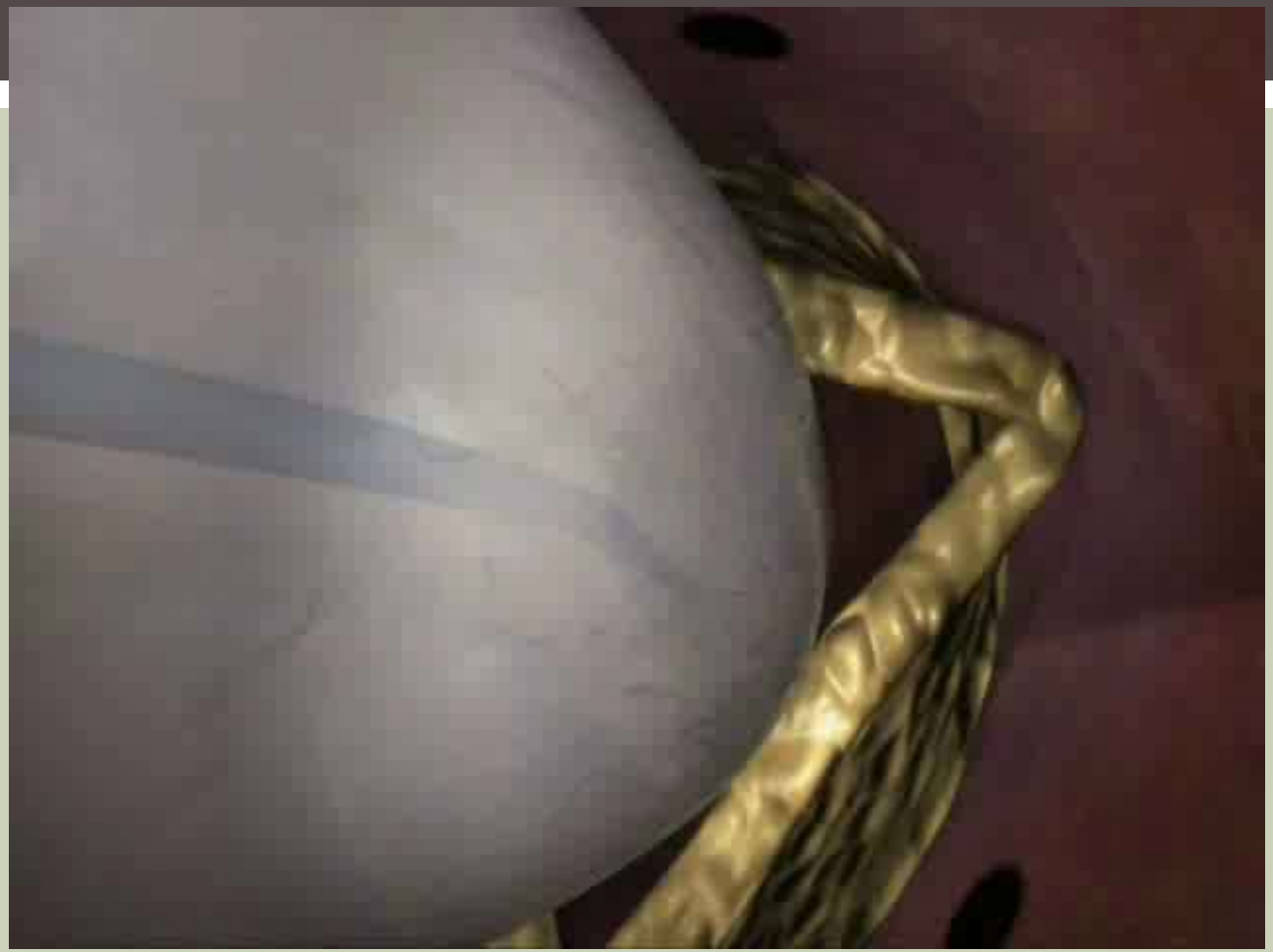
ANNULAR SIZE

CoreValve® Evolut™	CoreValve®		
			
23 mm	26 mm	29 mm	31 mm
18-20 mm	20-23 mm	23-26 mm	26-29 mm

CoreValve Delivery Catheter



COREVALVE in Delivery Catheter



CoreValve® US Pivotal Trial Inclusion Criteria

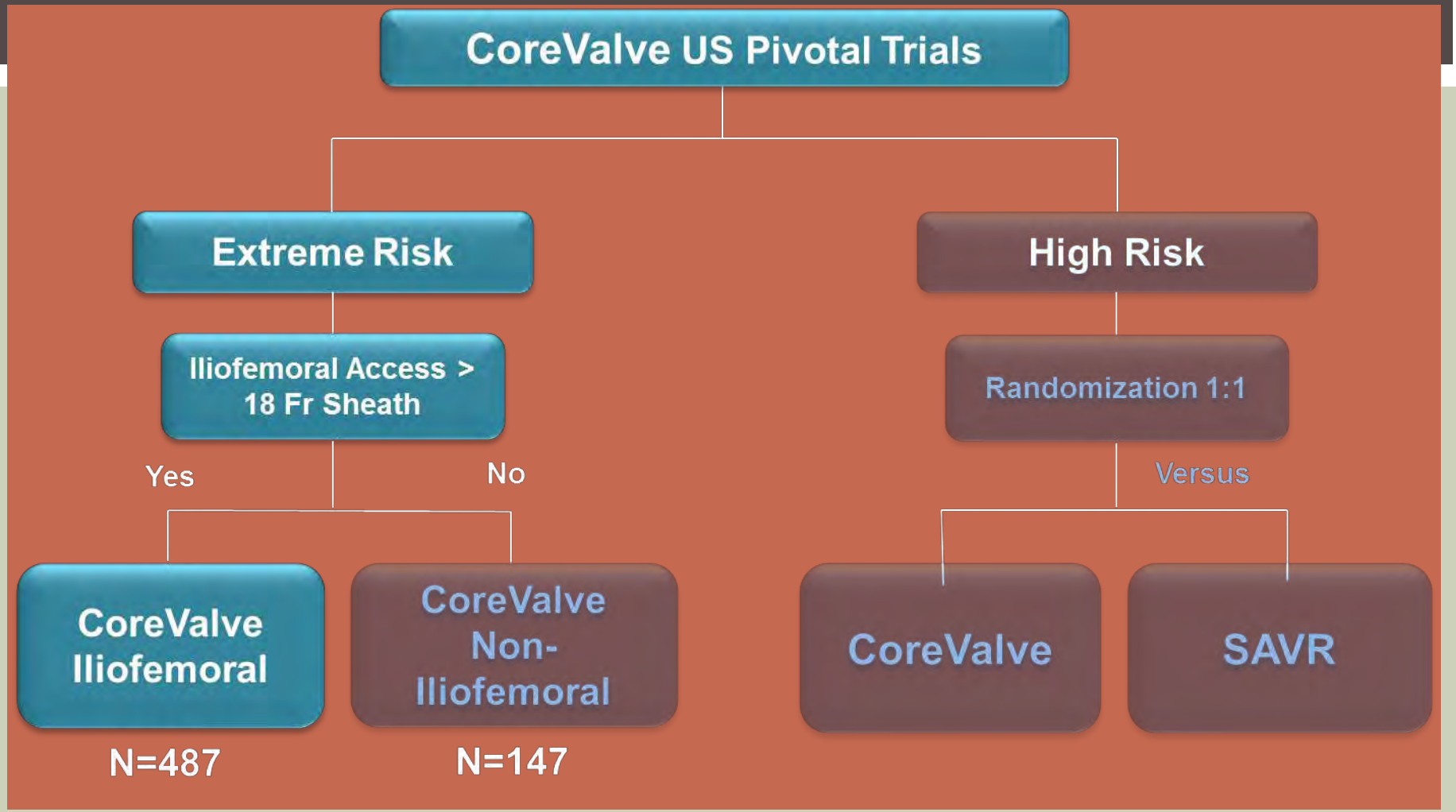
- **Extreme Risk : subjects with symptomatic severe AS, necessitating aortic valve replacement, with predicted operative mortality or serious, irreversible morbidity risk of ≥ 50% at 30 days**
- **High Risk : Subjects with symptomatic severe AS, necessitating aortic valve replacement, whose predicted risk of operative mortality is ≥ 15% (and whose predicted operative mortality or serious, irreversible morbidity risk is < 50%) at 30 days**

CoreValve® US Pivotal Trial Inclusion Criteria

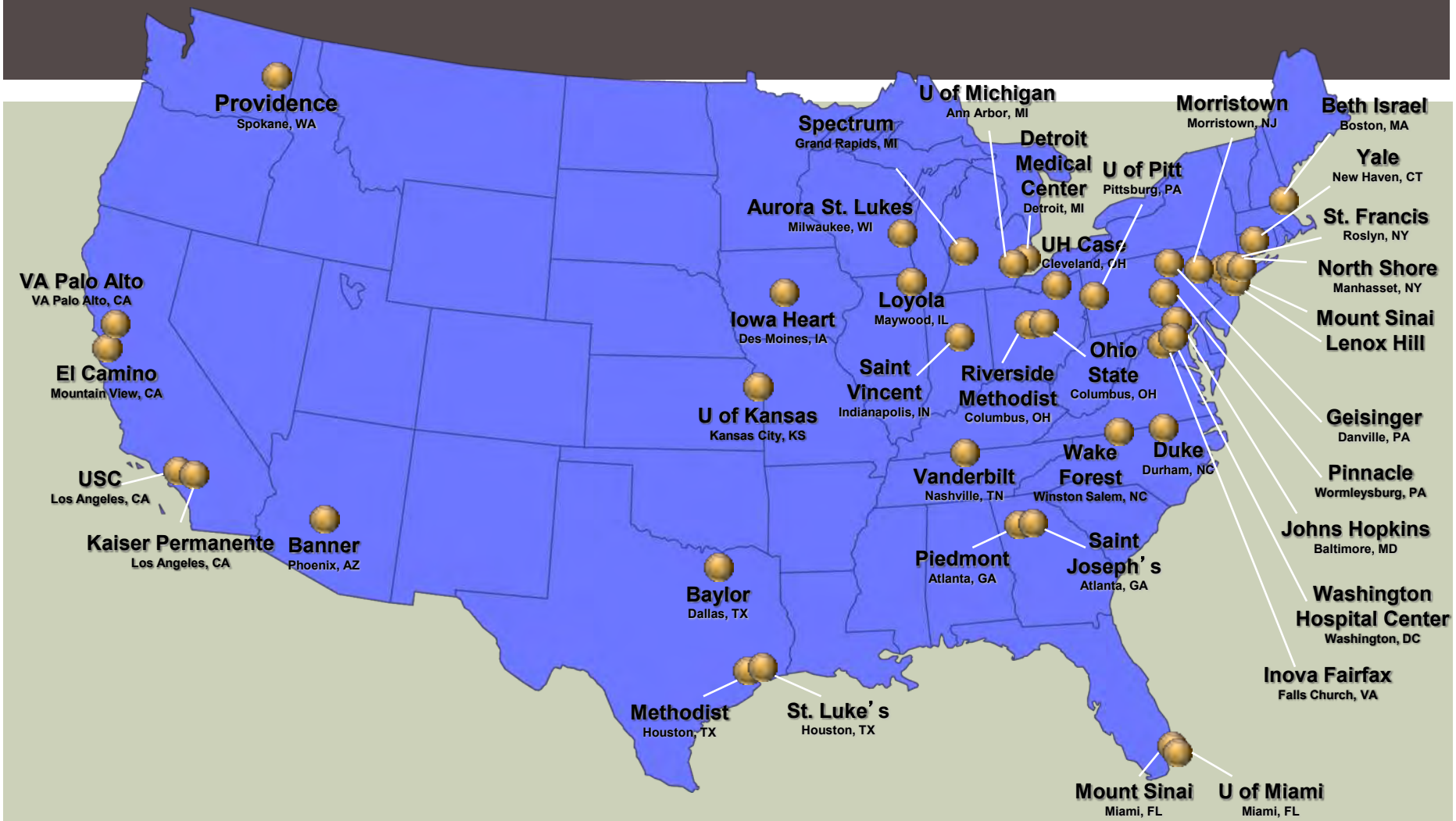
- Subject has senile degenerative aortic valve stenosis with
  - Mean gradient > 40 mm Hg or jet velocity > 4.0 m/s by either resting or dobutamine stress echocardiogram

  AND
  - An initial AVA of ≤ 0.8 cm^2 (or aortic valve area index ≤ 0.5 cm^2/m^2) by resting echocardiogram or catheterization
- Subject is symptomatic from his/her aortic valve stenosis as demonstrated by NYHA class II or greater

Pivotal Trial Design



Participating Sites



487 Patients Enrolled at 40 Participating Sites

BASELINE DEMOGRAPHICS

Characteristic	N=471
Age, years	83.1 ± 8.6
Men, %	49.0
STS Predicted Risk of Mortality, %	10.3 ± 5.6
Logistic EuroSCORE, %	22.7 ± 17.4
New York Heart Association (NYHA)	
NYHA Class III/IV, %	91.9
Diabetes Mellitus, %	42.5
Insulin Requiring Diabetes, %	19.1
Prior Stroke, %	13.8
Modified Rankin 0 or 1, %	71.9
Modified Rankin > 1, %	28.1

PROHIBITIVE CHEST ANATOMY

Characteristic	N=471
Any Anatomic Characteristic, %	31.7
Aorta Calcification*, %	
Severe, %	17.2
Porcelain, %	4.9
Hostile Mediastinum, %	11.5
Chest Wall Deformity, %	5.1

***Aorta calcification is measured on screening CT angiogram**

BASELINE CO-MORBIDITIES

Co-Morbidity Assessment	N=471
Any Chronic Lung Disease (STS Criteria), %	58.8
Moderate, %	15.3
Severe*, %	24.0
Home Oxygen, %	30.4
FEV1 ≤ 1000 cc, %	23.1
Diffusion Capacity < 50%, %	22.3
Charlson Co-Morbidity Score**, %	5.3 ± 2.3
Moderate (3, 4), %	32.9
Severe (≥ 5), %	58.6

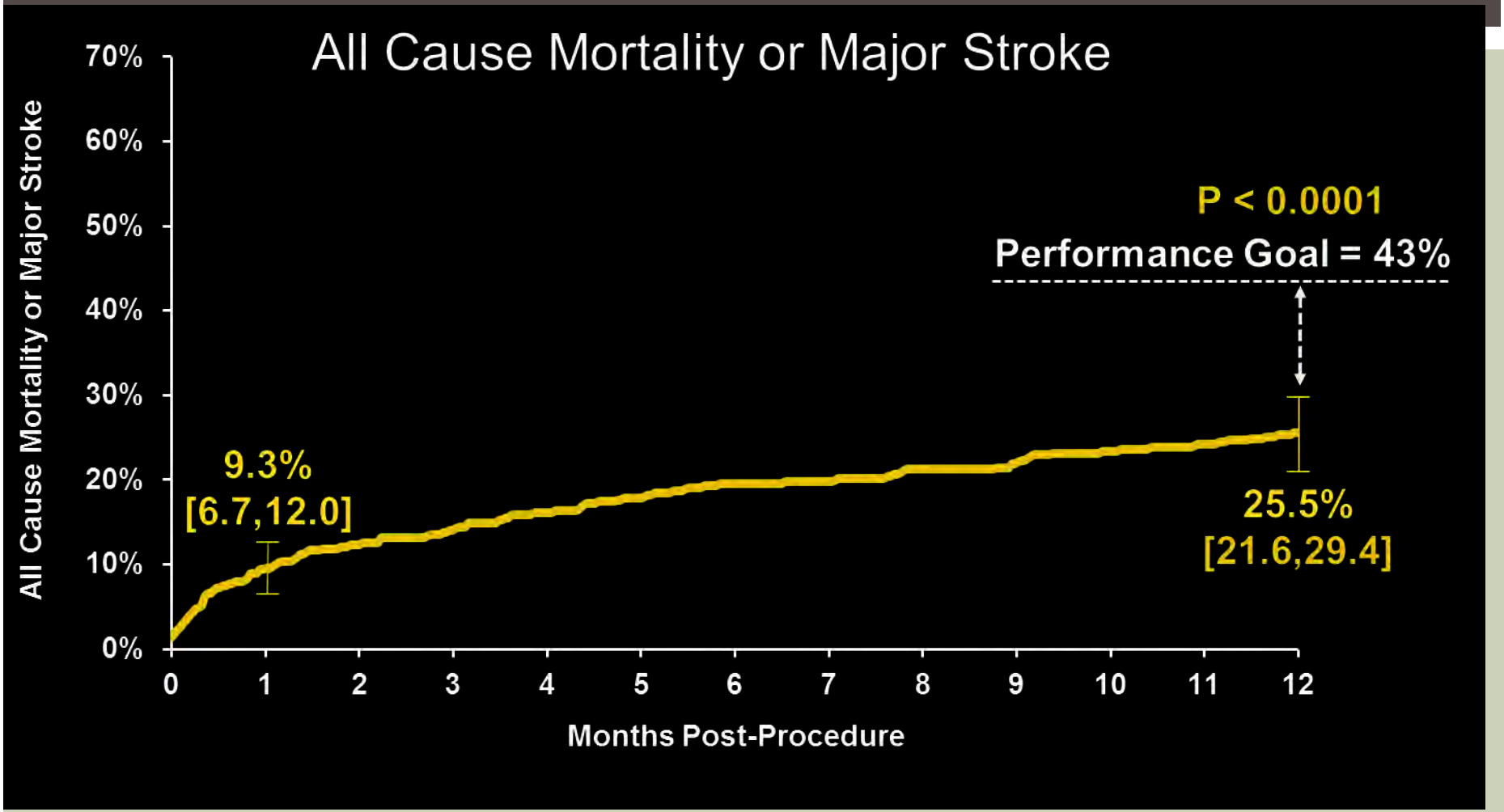
**Charlson Score: = 1 MI, CHF, PVD, CVD, dementia, chronic lung disease, connective tissue disease, ulcer, mild liver disease, DM; = 2 hemiplegia, mod-severe kidney disease, diabetes with end organ damage, leukemia, lymphoma; = 3 moderate or severe liver disease; = 6 metastatic solid tumor, AIDS

FRAILTY ASSESSMENT

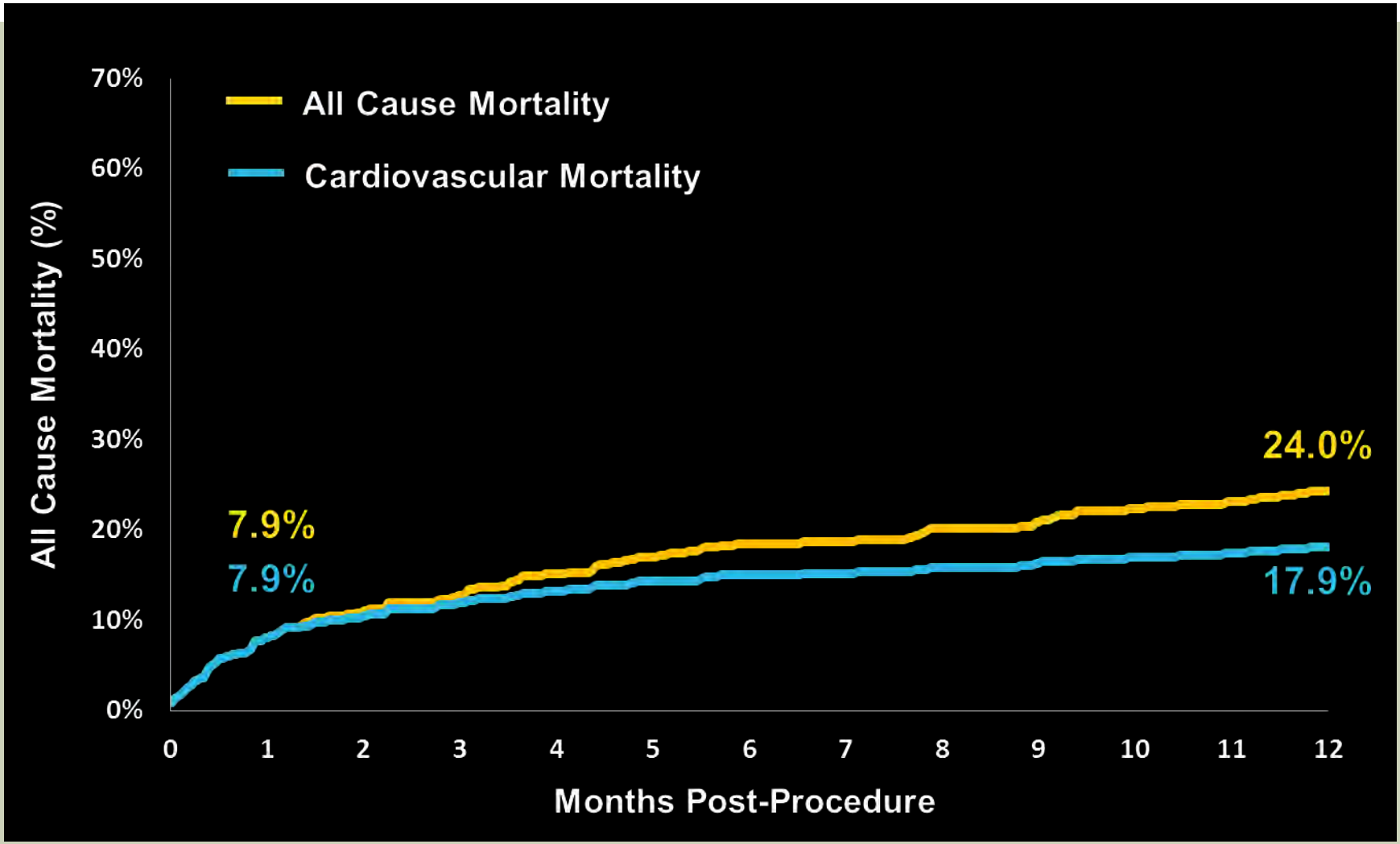
Frailty Characteristic	N=471
Anemia With Prior Transfusion, %	22.9
BMI < 21 kg/m^2, %	7.6
Albumin < 3.3 g/dL, %	18.5
Unplanned Weight Loss > 10 pounds, %	16.9
Falls in Past 6 Months, %	17.8
5 Meter Gait Speed > 6 secs, %	84.2
Grip Strength < Threshold, %	67.6

COREVALVE EXTREME RISK ILIOFEMORAL RESULTS

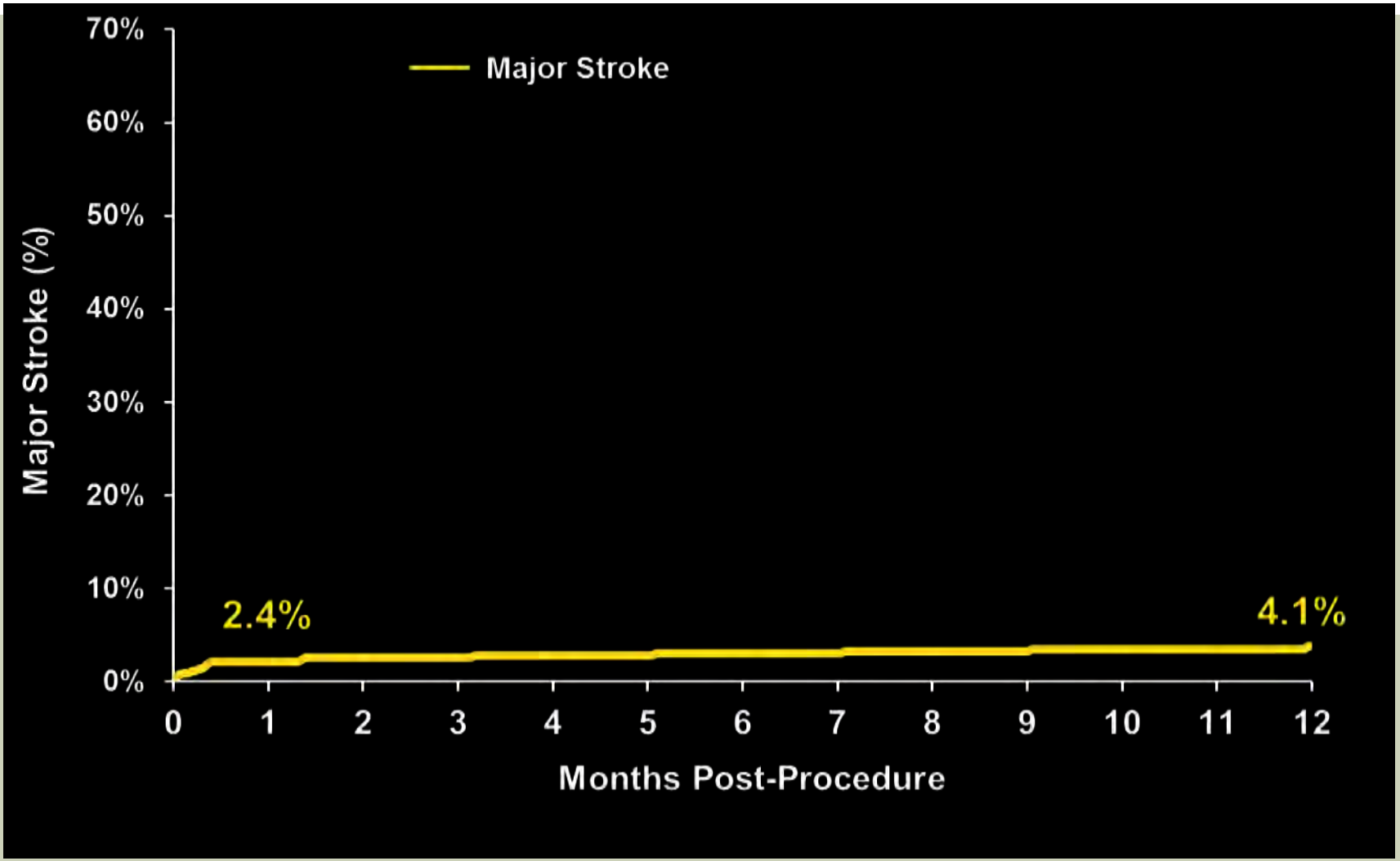
Primary Endpoint



1 Year Mortality

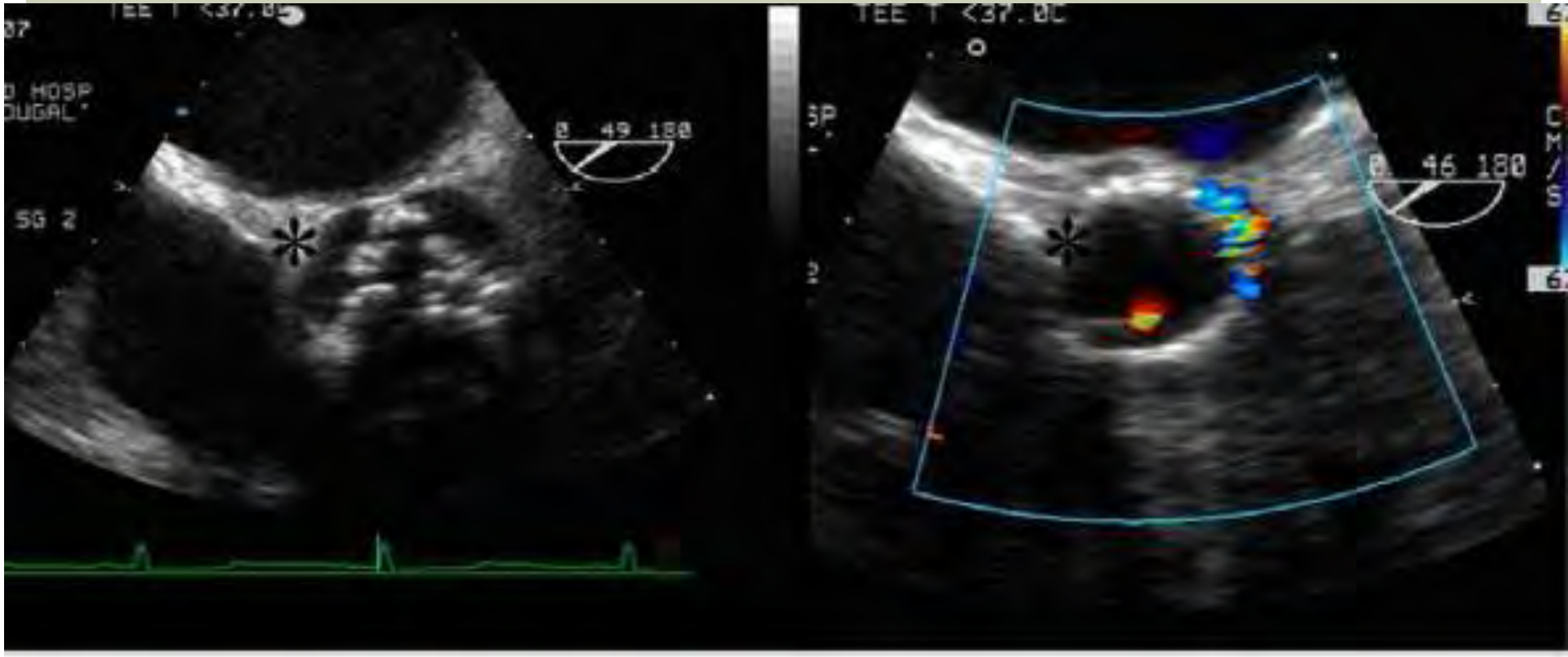


Major Stroke



Secondary Endpoints

Events*	1 Month	1 Year
Any Stroke, %	3.9	6.7
Major, %	2.4	4.1
Minor, %	1.7	3.1
Myocardial Infarction, %	1.3	2.0
Reintervention, %	1.3	2.0
VARC Bleeding, %	35.1	41.4
Life Threatening or Disabling, %	11.7	16.6
Major, %	24.1	27.6
Major Vascular Complications, %	8.3	8.5
Permanent Pacemaker Implant, %	22.2	27.1
Per ACC Guidelines, %	17.4	19.9

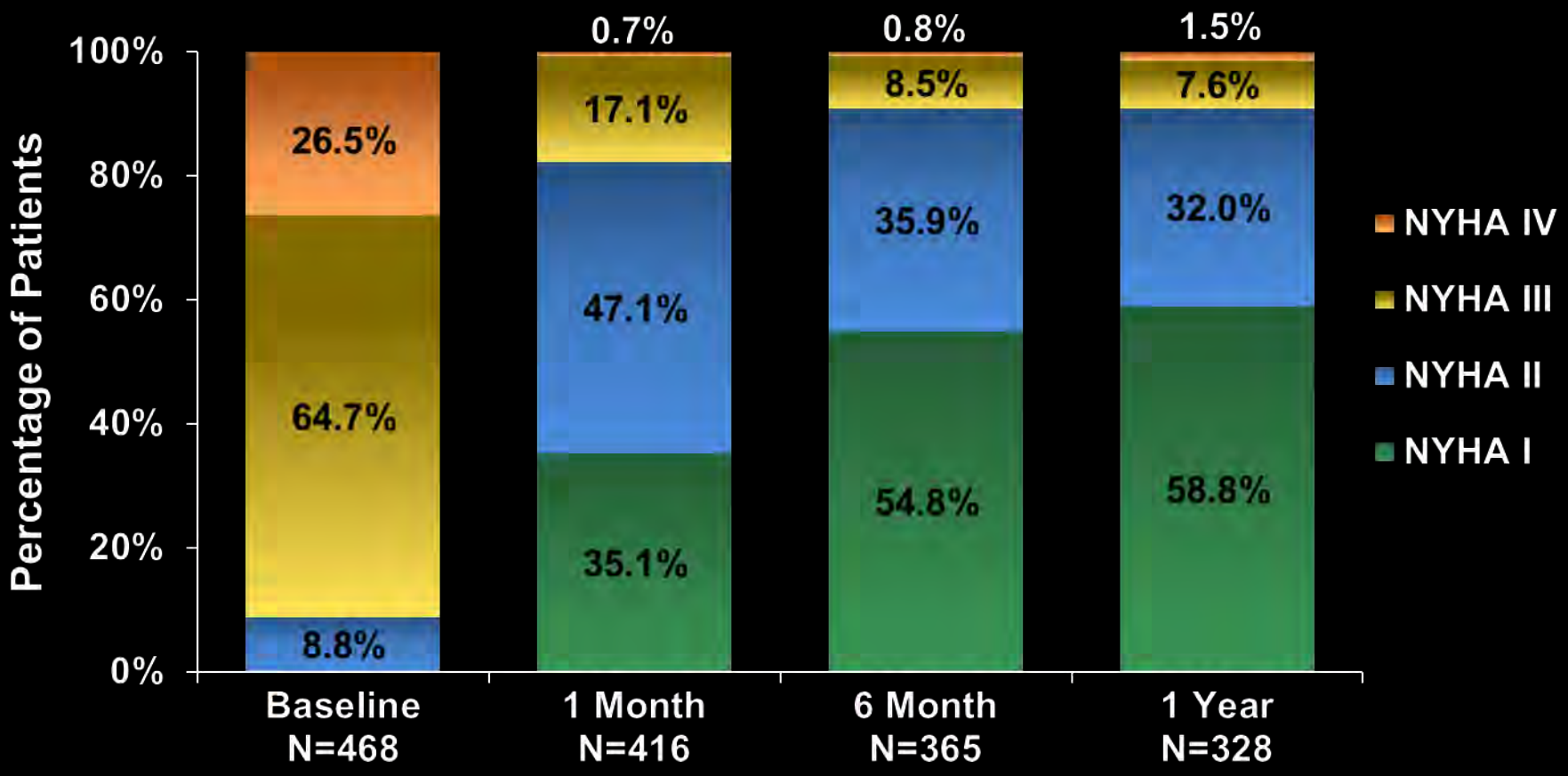


*Left bundle travels through the central fibrous body next to the Non-coronary Cusp

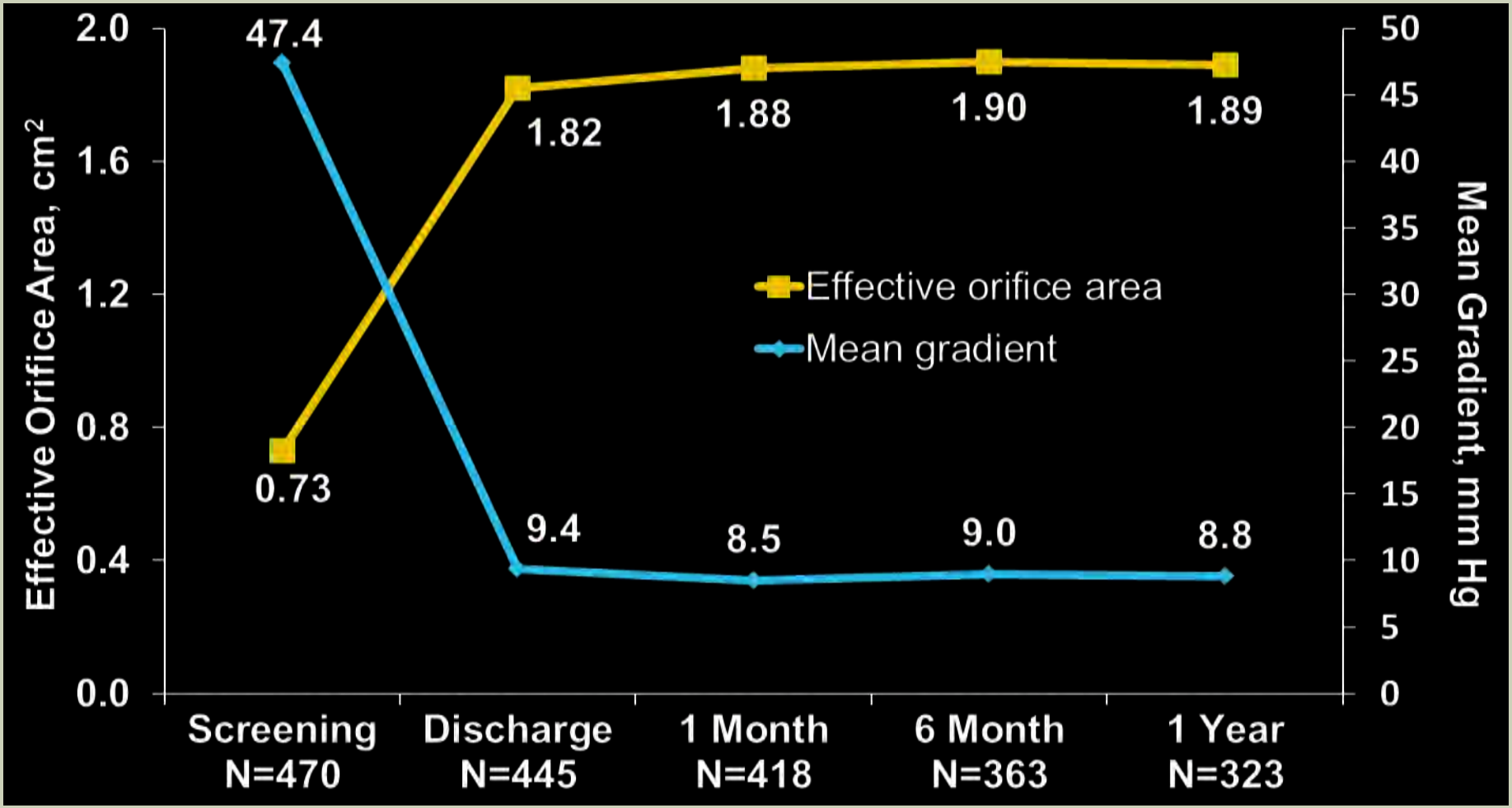
NYHA CLASS SURVIVORS

90% of Patients Improved at Least 1 NYHA Class by 1 Year

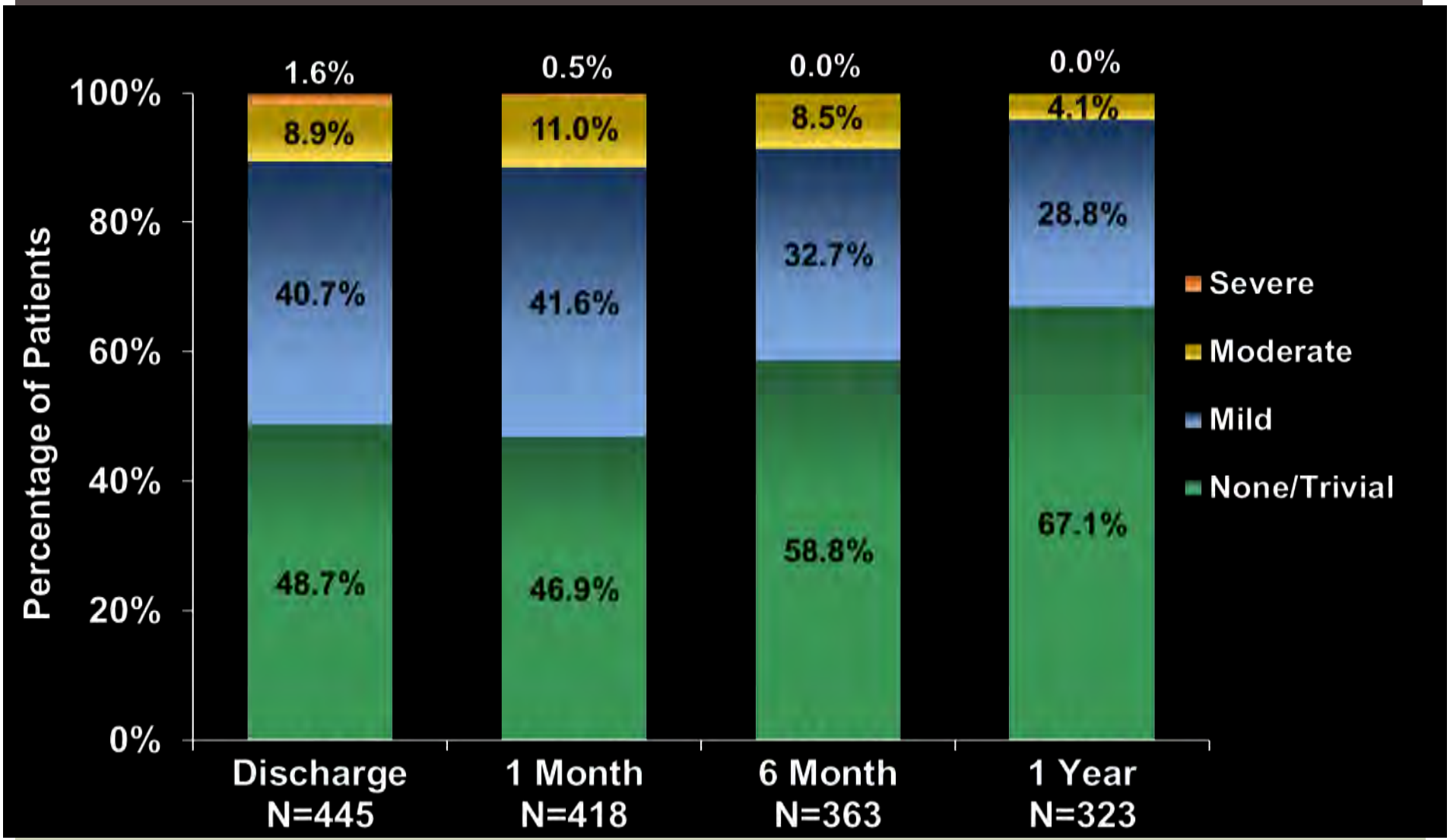
60% of Patients Improved at Least 2 NYHA Classes by 1 Year



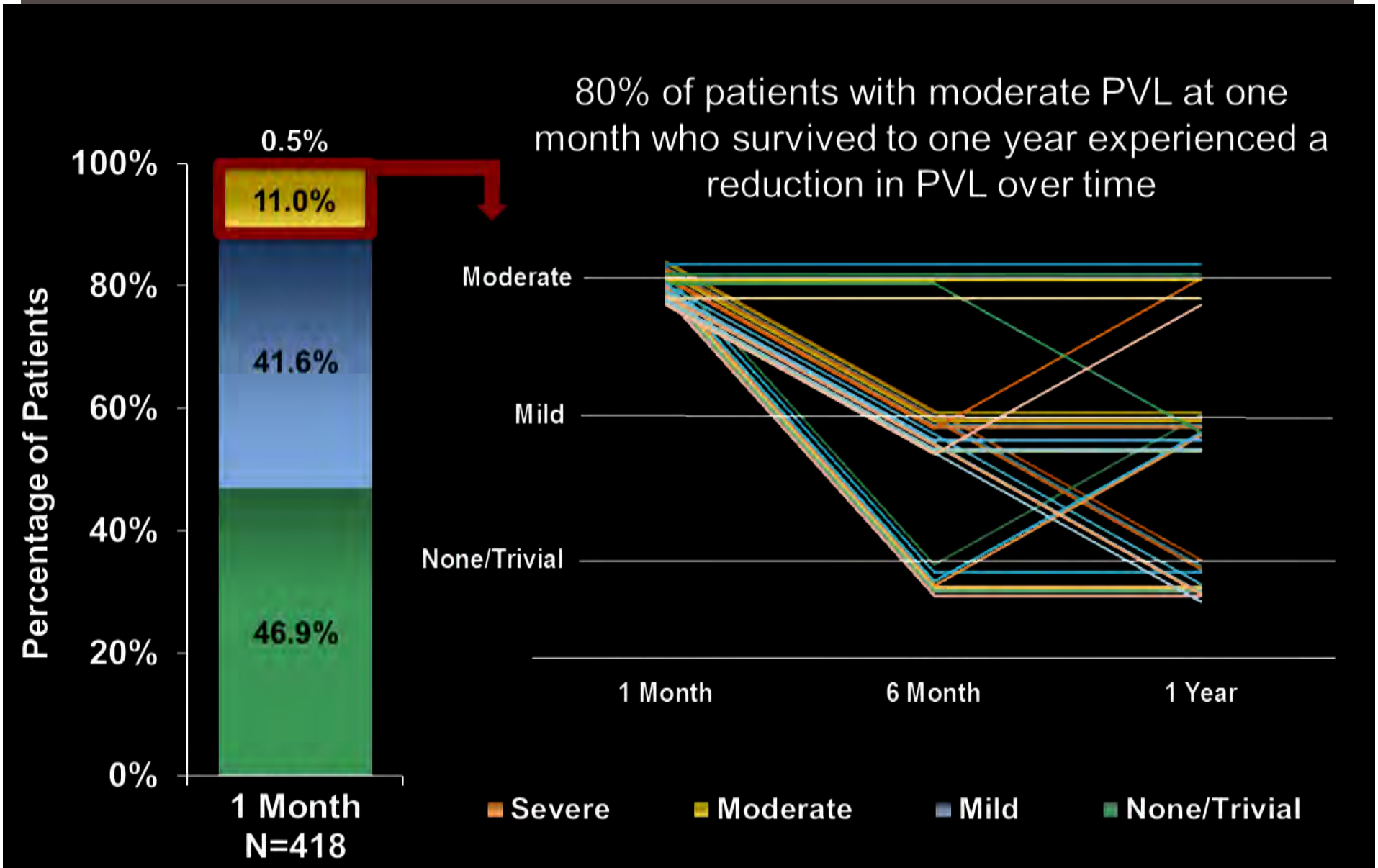
ECHOCARDIOGRAPHIC FINDINGS



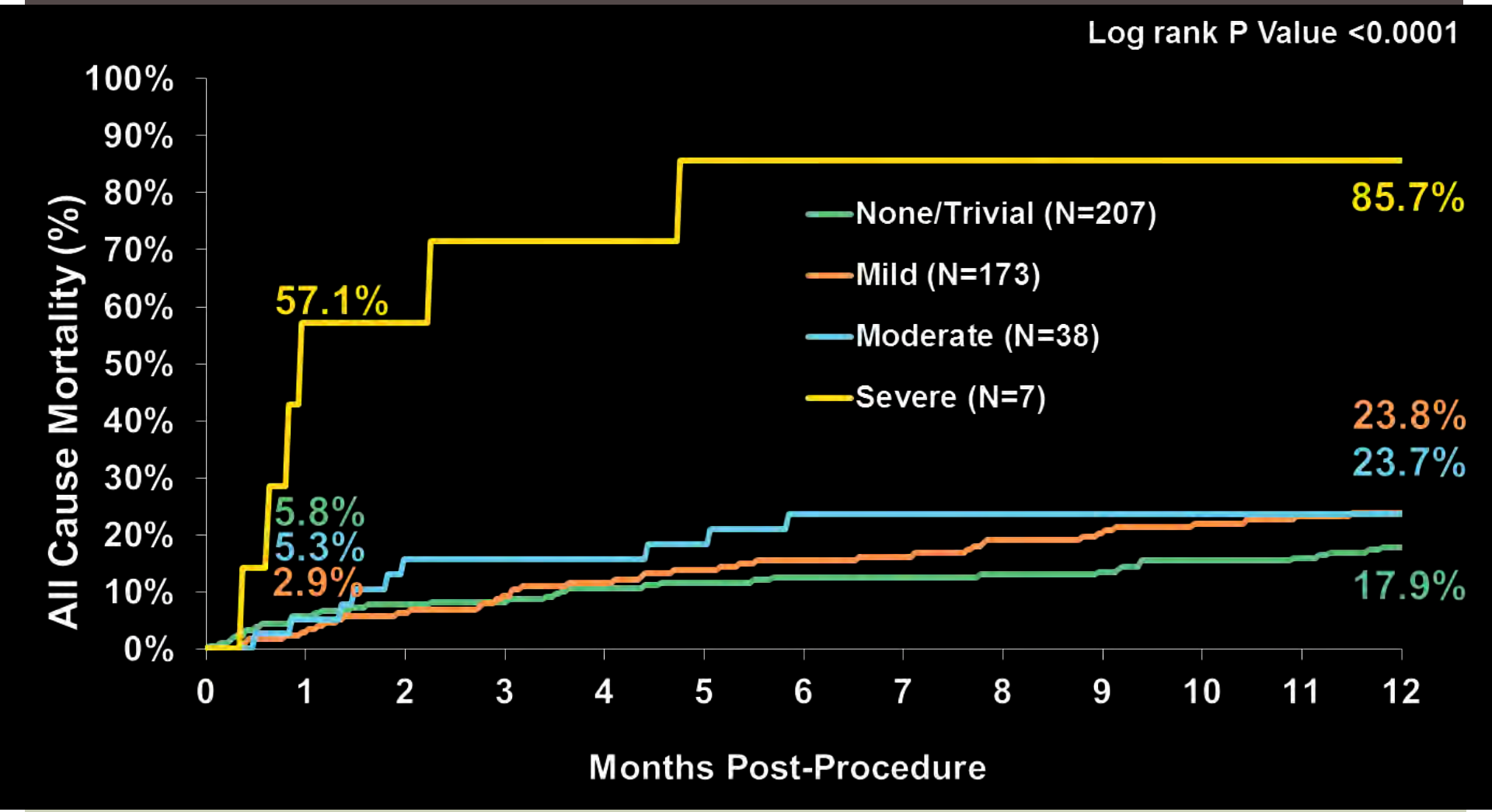
Paravalvular Regurgitation



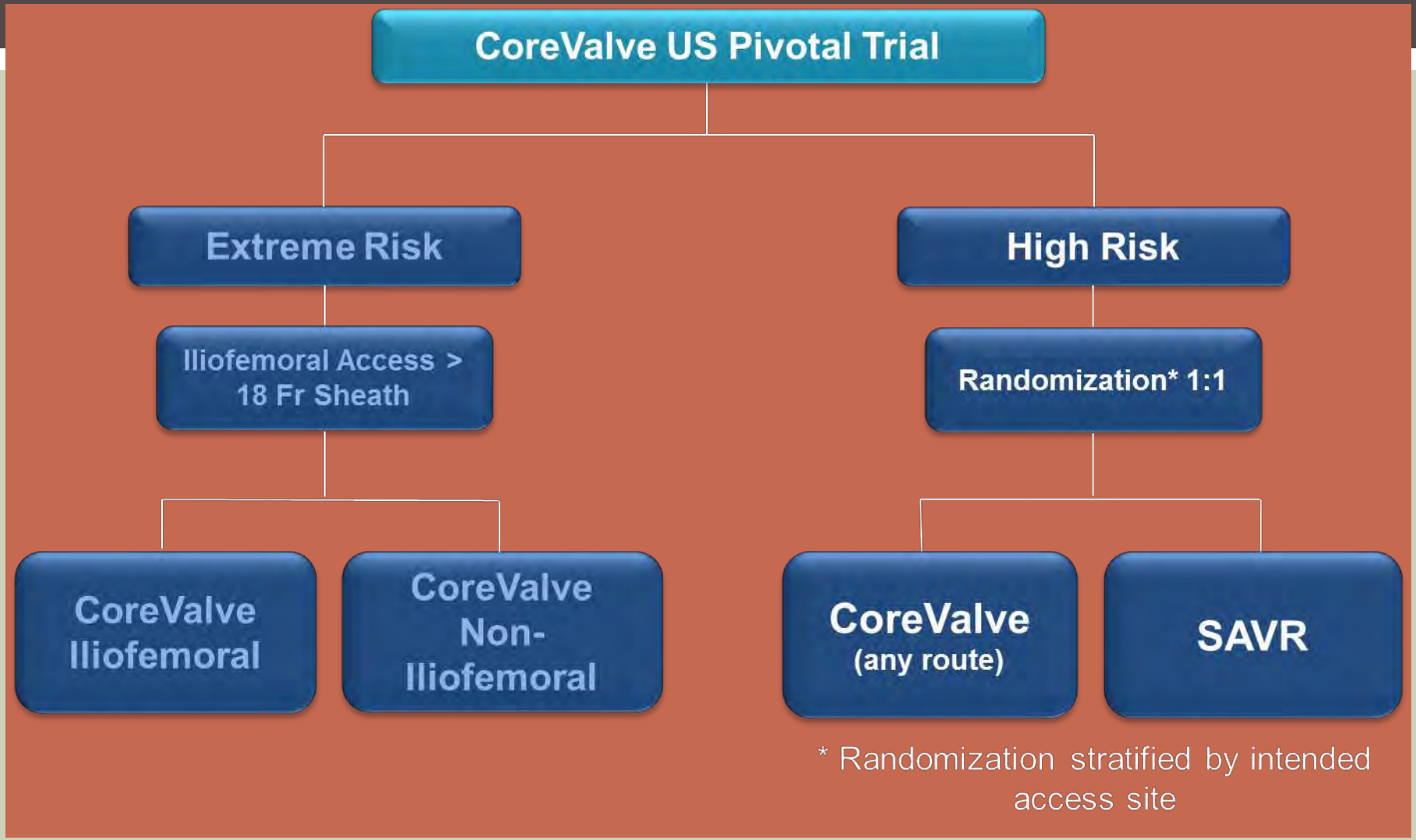
Paravalvular Regurgitation



Impact of PVL on Late Mortality



Pivotal Trial Design



* Randomization stratified by intended access site

Primary Endpoint

Primary Endpoint: All-cause mortality at 1 year

Non-inferiority Testing: TAVR with the CoreValve prosthesis was non-inferior to SAVR for 1 year all-cause mortality with a 7.5% non-inferiority margin

Superiority Testing: If the primary endpoint was met at the one-sided 0.05 level, a subsequent test for superiority was performed at the one-sided 0.05 level

Inclusion Criteria

- **NYHA functional class II or greater**
- **Severe aortic stenosis: AVA ≤ 0.8 cm^2 or AVAI ≤ 0.5 cm^2/m^2 AND mean gradient > 40 mm Hg or peak velocity > 4 m/sec at rest or with dobutamine stress echocardiogram**

Inclusion Criteria

- **Risk of death at 30 days after surgery was ≥ 15% and the risk of death or irreversible complications within 30 days was < 50%**
- **Surgical risk assessment included consideration of STS Predicted Risk of Mortality estimate and other risk factors not captured in the STS risk model**

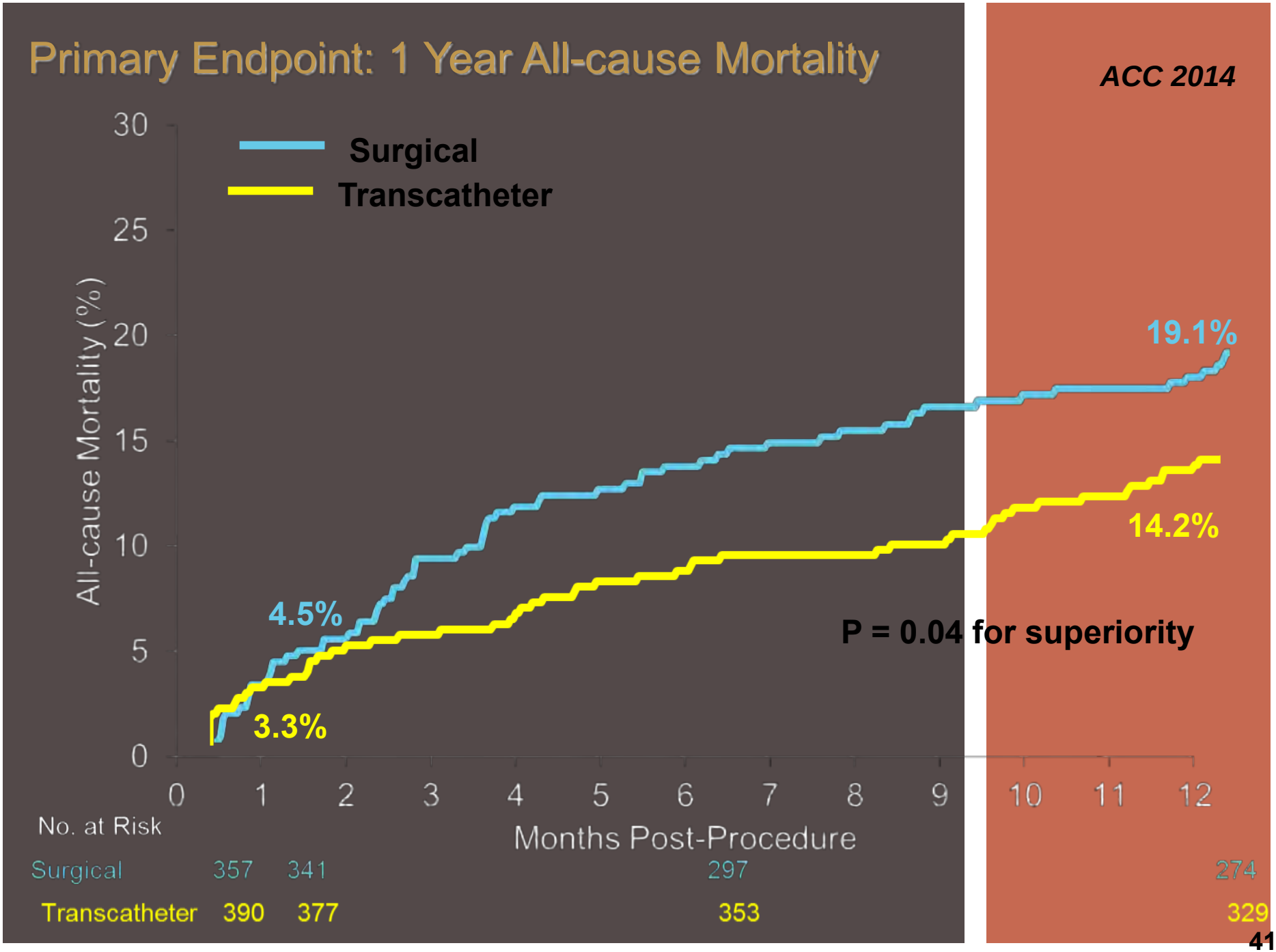
Baseline Demographics

Characteristic	TAVR N=390	SAVR N=357
Age, years	83.1 ± 7.1	83.2 ± 6.4
Men, %	53.1	52.4
STS Predicted Risk of Mortality, %	7.3 ± 3.0	7.5 ± 3.4
Logistic EuroSCORE, %	17.7 ± 13.1	18.6 ± 13.0
NYHA Class III/IV, %	85.6	86.8
Prior Coronary-artery Bypass Surgery	29.5	31.1
Diabetes Mellitus, %	34.9*	45.4*
Insulin Requiring Diabetes, %	11.0	13.2
Prior Stroke, %	12.6	14.0
Modified Rankin 0 or 1, %	74.5	87.2
Modified Rankin > 1, %	25.5	12.8
STS Severe Chronic Lung Disease, %	13.3	9.0

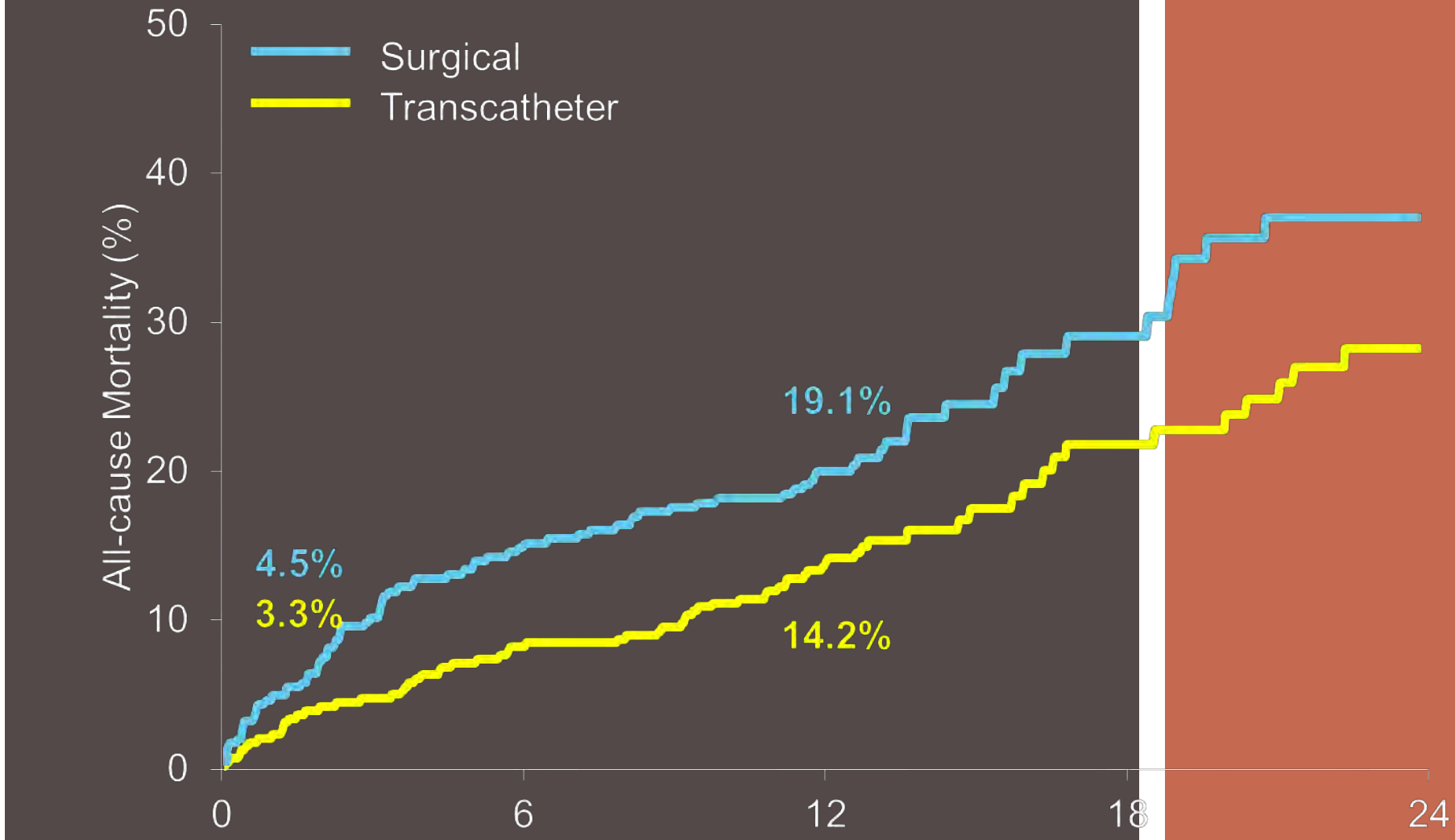
*P < 0.01

Primary Endpoint: 1 Year All-cause Mortality

ACC 2014

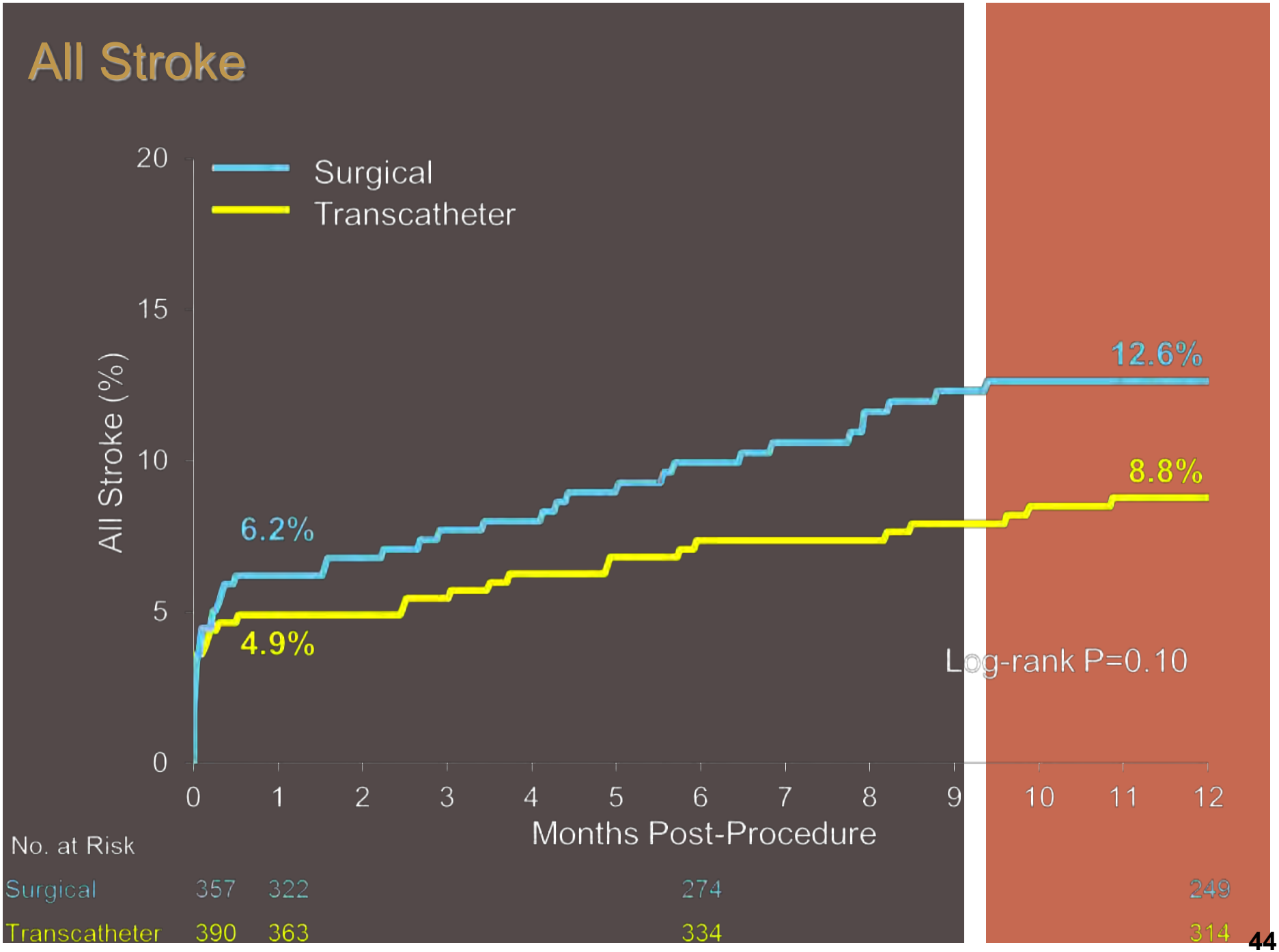


2-Year All-cause Mortality

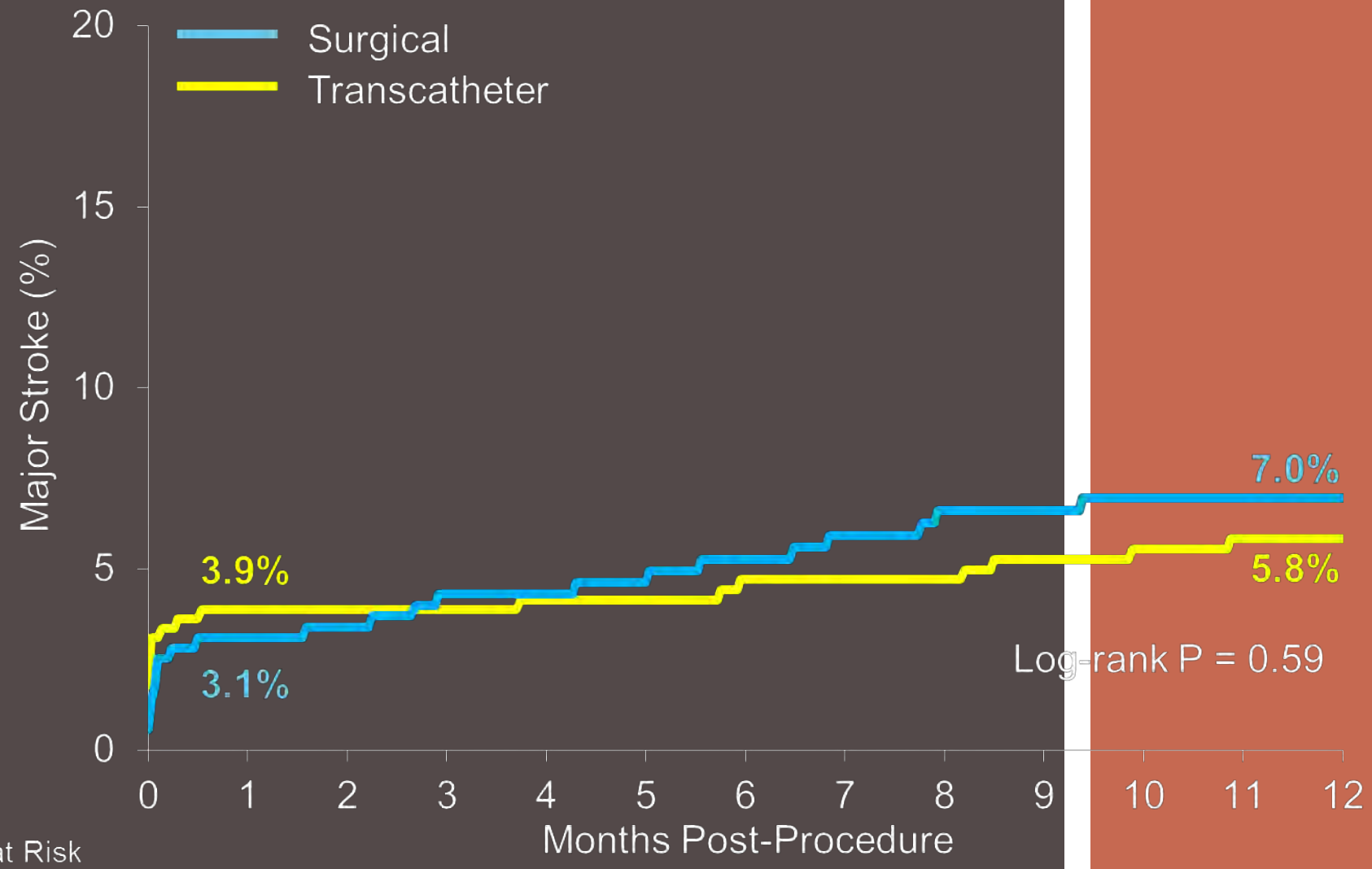


No. at Risk				
Surgical	357	341	274	28
Transcatheter	390	377	329	38

All Stroke

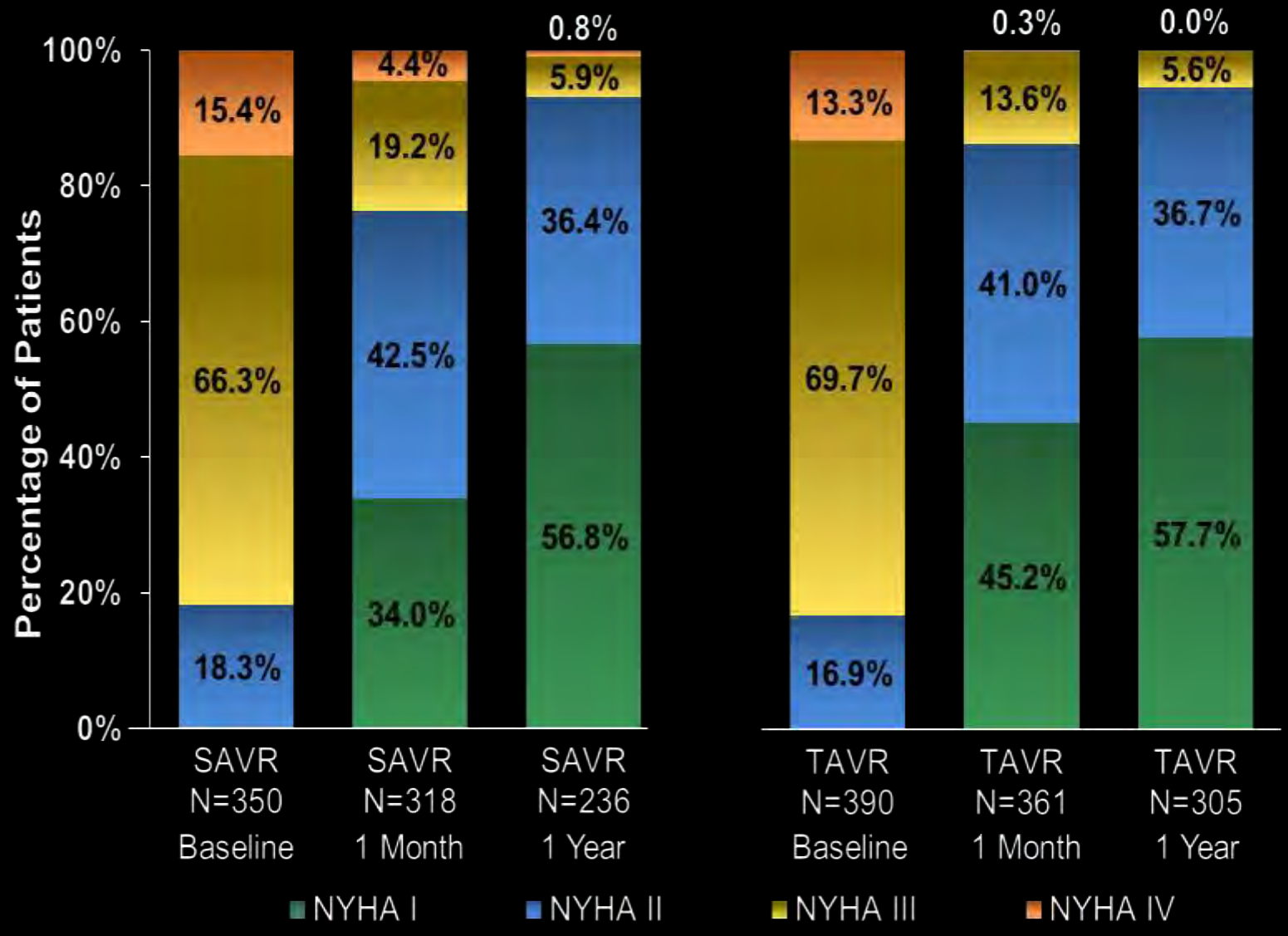

Surgical
Transcatheter
All Stroke (%)
20
15
10
5
0
12.6%
8.8%
6.2%
4.9%
Log-rank P=0.10
0
1
2
3
4
5
6
7
8
9
10
11
12
Months Post-Procedure
No. at Risk
Surgical 357 322 274 249
Transcatheter 390 363 334 314

Major Stroke

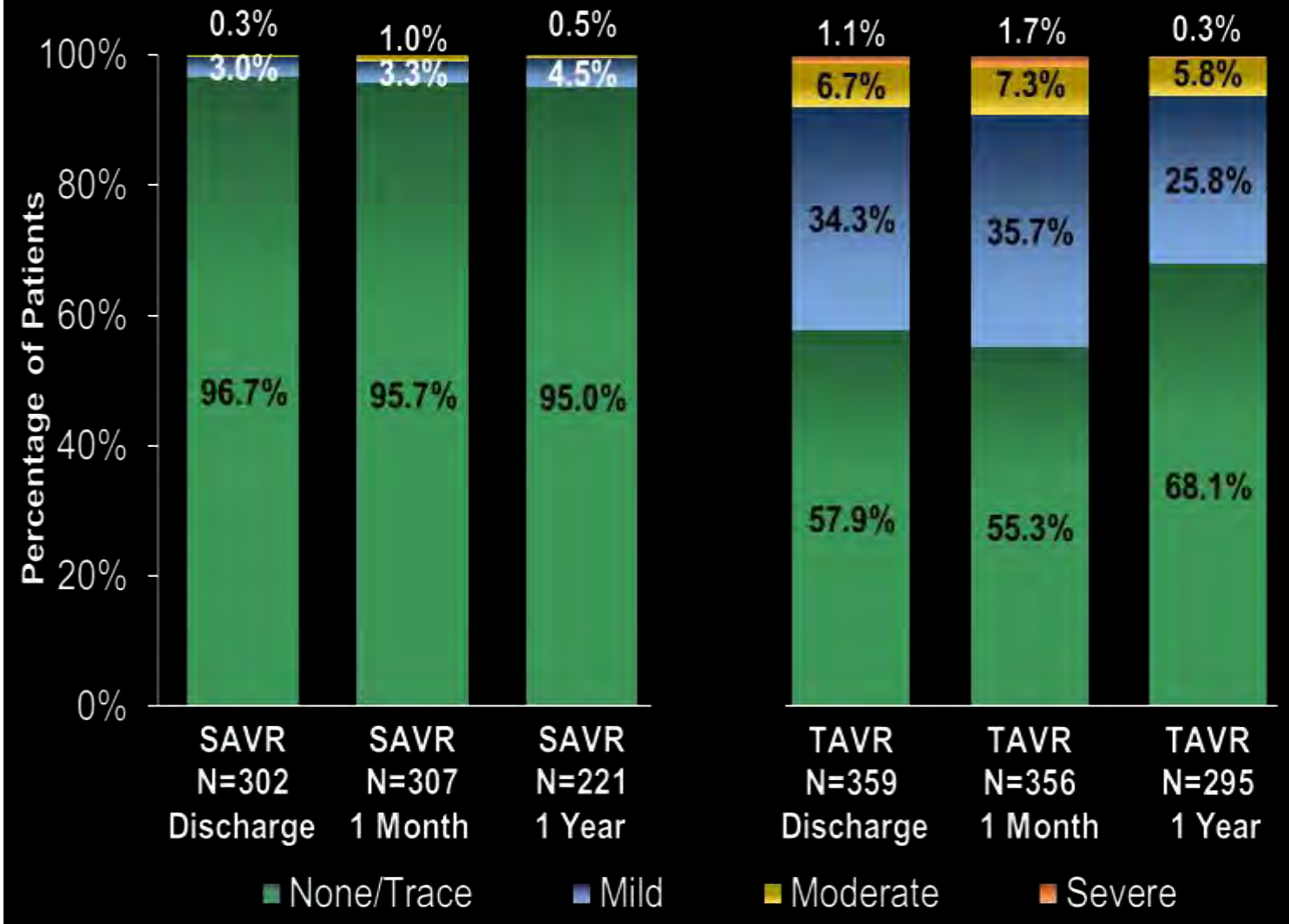


No. at Risk					
Surgical	357	333	289		263
Transcatheter	390	367	344		322

NYHA CLASS SURVIVORS

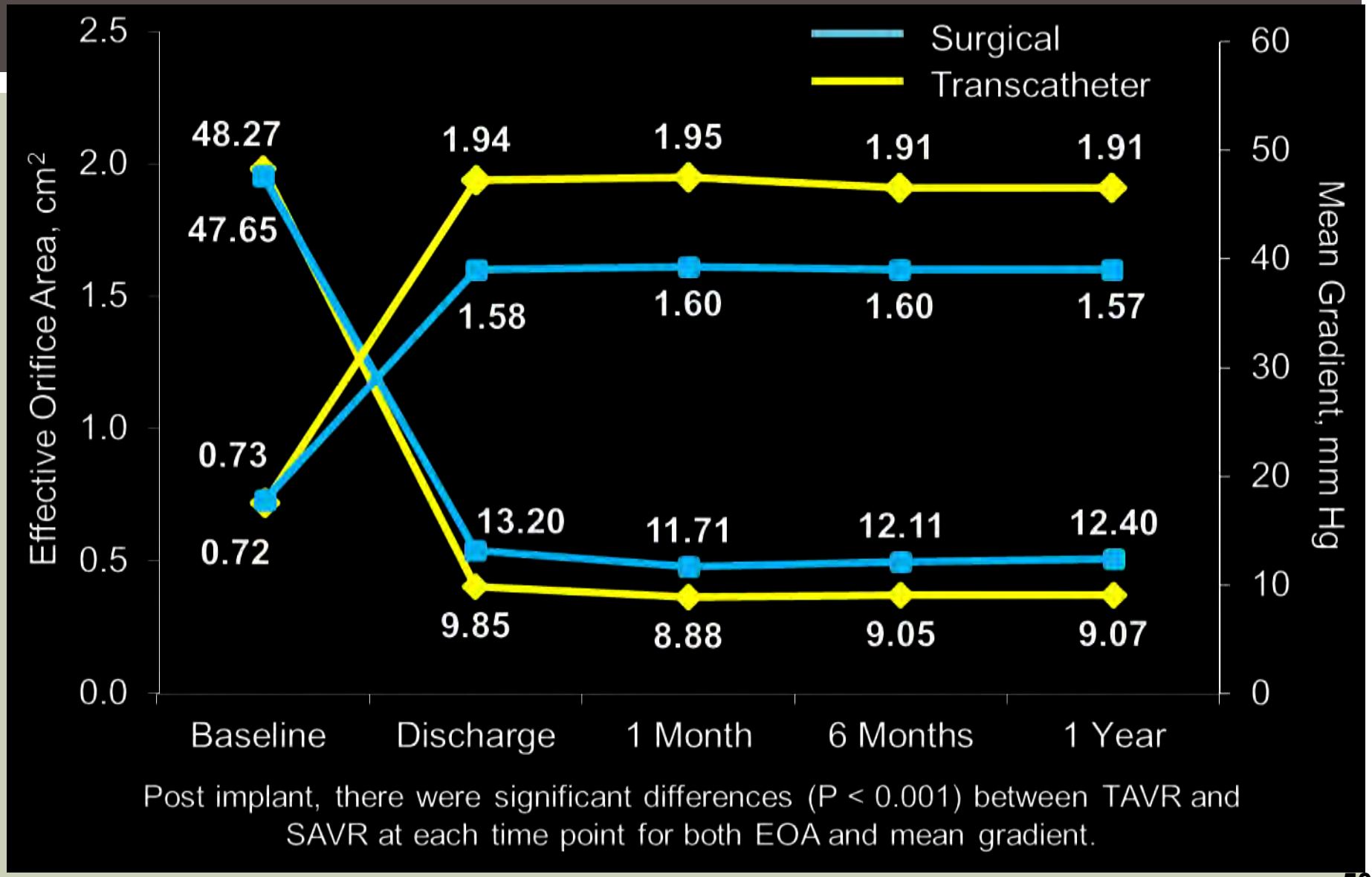


Paravalvular Regurgitation



There was significantly lower PVL with SAVR over TAVR at each time point (P<0.001)

ECHOCARDIOGRAPHIC FINDINGS



Post implant, there were significant differences ($P < 0.001$) between TAVR and SAVR at each time point for both EOA and mean gradient.

Thank You