TCT-AP 2017
Seoul, April 25-28, 2017

Ongoing TAVR Trials and Updating TAVR Guidelines

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Physician Name	Company/Relationship
Speaker Bureau/Advisory Board:	Medtronic: C, SB, AB, OF LivaNova: C, SB, AB Highlife: AB, SB Boston Scientific: C, SB, AB Millipede: SB, C Pipeline: SB,C
Equity Interest:	InSeal Medical: E, AB, Valtech: E, SB, Claret: E, AB Shockwave: E, AB Valve Medical: E, AB Mitra/Trialign E, AB, SB

Key

G – Grant and or Research Support E – Equity Interests S – Salary, AB – Advisory Board
C – Consulting fees, Honoraria R – Royalty Income I – Intellectual Property Rights
SB – Speaker's Bureau O – Ownership OF – Other Financial Benefits

Guidelines: Heart Team

Recommendations for Choice of Intervention			
COR	**LOE**	**Recommendations**	**Comment/Rationale**
I	**C**	**For patients in whom TAVR or high-risk surgical AVR is being considered, a heart valve team consisting of an integrated, multidisciplinary group of healthcare professionals with expertise in VHD, cardiac imaging, interventional cardiology, cardiac anesthesia, and cardiac surgery should collaborate to provide optimal patient care.**	2014 recommendation remains current.

Nishimura et al. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease. Circulation 2017 Mar 15

Guidelines:
TAVR in Patients at Extreme Surgical Risk

2017 Update

I	A	**TAVR is recommended for symptomatic patients with severe AS (Stage D) and a prohibitive risk for surgical AVR who have a predicted post-TAVR survival greater than 12 months (58-61).**	**MODIFIED: LOE updated from B to A.** Longer-term follow-up from RCTs and additional observational studies has demonstrated the benefit of TAVR in patients with a prohibitive surgical risk.
See Online Data Supplements 5 and 9 (Updated From 2014 VHD Guideline)			

Nishimura et al. 2017 AHA/ACC Focuesed Update of the 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease. Circulation 2017 Mar 15

Patients at Extreme Surgical Risk

Foundational trials tested new TAVR therapy in patients without the option for a surgical aortic valve replacement

US CoreValve Pivotal Trial

CoreValve, N=489, STS 10.3%

Transcatheter Aortic Valve Replacement Using a Self-Expanding Bioprosthesis in Patients With Severe Aortic Stenosis at Extreme Risk for Surgery

Jeffrey J. Popma, MD,* David H. Adams, MD,† Michael J. Reardon, MD,† Steven J. Yakubov, MD,† Neal S. Kleiman, MD,† David Heimansohn, MD,† James Hermiller, Jr, MD,† G. Chad Hughes, MD,¶ J. Kevin Harrison, MD,¶ Joseph Coselli, MD,# Jose Diez, MD,# Ali Kafi, MD,** Theodore Schreiber, MD,** Thomas G. Gleason, MD,†† John Conte, MD,†† Maurice Buchbinder, MD,†† G. Michael Deeb, MD,††† Blasé Carabello, MD,¶¶ Patrick W. Serruys, MD, PhD,## Sharla Chenoweth, MS,*** Jae K. Oh, MD,††† for the CoreValve United States Clinical Investigators

Boston, Massachusetts; New York, New York; Houston, Texas; Columbus, Ohio; Indianapolis, Indiana; Durham, North Carolina; Detroit and Ann Arbor, Michigan; Pittsburgh, Pennsylvania; Baltimore, Maryland; Palo Alto, California; Rotterdam, the Netherlands; and Minneapolis and Rochester, Minnesota

PARTNER 1B

SAPIEN, N=179, STS 11.2%

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 21, 2010 VOL. 363 NO. 17

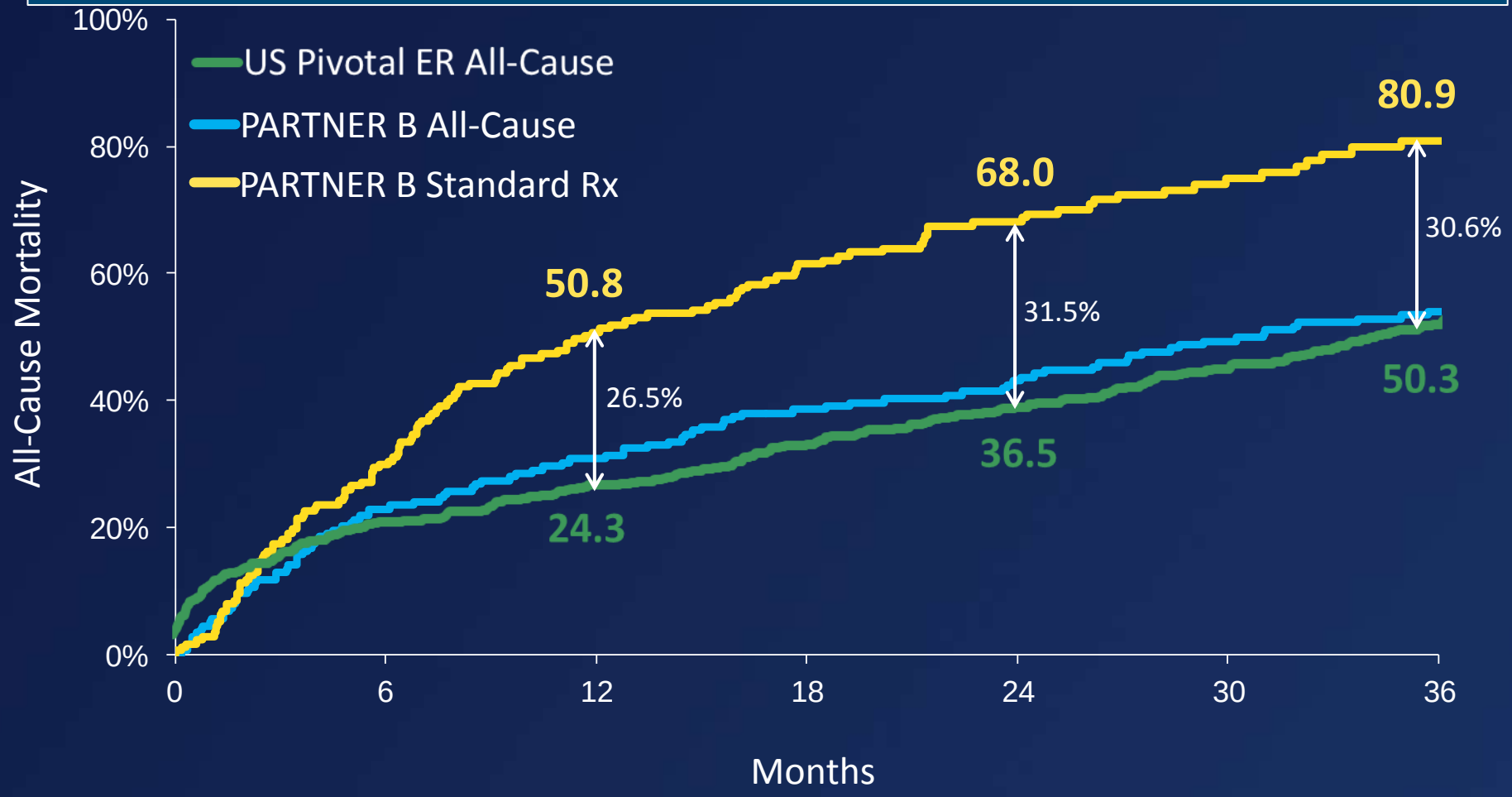
Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela S. Douglas, M.D., John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators*

Patients at Extreme Surgical Risk

3-Year Follow-Up

- PARTNER showed that by 3 years, TAVR had reduced mortality by approximately 30% compared to standard medical management.
- Similar survival results were achieved with CoreValve in the US Pivotal Trial



Guidelines: TAVR in Patients at High Surgical Risk

2017 Update

I	A	**Surgical AVR or TAVR is recommended for symptomatic patients with severe AS (Stage D) and high risk for surgical AVR, depending on patient-specific procedural risks, values, and preferences (49-51).**	**MODIFIED: COR updated from IIa to I, LOE updated from B to A.** Longer-term follow-up and additional RCTs have demonstrated that TAVR is equivalent to surgical AVR for severe symptomatic AS when surgical risk is high.
See Online Data Supplement 9 (Updated From 2014 VHD Guideline)			

Nishimura et al. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease. Circulation 2017 Mar 15

Patients at High Surgical Risk

Trials randomizing high risk patients to either TAVR or SAVR soon followed

US CoreValve Pivotal Trial

CoreValve, N=390, STS 7.3% vs.
SAVR, N=357, STS 7.5%

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement with a Self-Expanding Prosthesis

David H. Adams, M.D., Jeffrey J. Popma, M.D., Michael J. Reardon, M.D., Steven J. Yakubov, M.D., Joseph S. Coselli, M.D., G. Michael Deeb, M.D., Thomas G. Gleason, M.D., Maurice Buchbinder, M.D., James Hermiller, Jr., M.D., Neal S. Kleiman, M.D., Stan Chetcuti, M.D., John Heiser, M.D., William Merhi, D.O., George Zorn, M.D., Peter Tadros, M.D., Newell Robinson, M.D., George Petrossian, M.D., G. Chad Hughes, M.D., J. Kevin Harrison, M.D., John Conte, M.D., Brijeshwar Maini, M.D., Mubashir Mumtaz, M.D., Sharla Chenoweth, M.S., and Jae K. Oh, M.D., for the U.S. CoreValve Clinical Investigators*

PARTNER 1A

SAPIEN, N=348, STS 11.8% vs.
SAVR, N=351, STS 11.7%

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 9, 2011 VOL. 364 NO. 23

Transcatheter and Surgical Aortic-Valve Replacement in High-Risk Patients

Craig R. Smith, M.D., Martin B. Leon, M.D., Michael J. Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., Mathew Williams, M.D., Todd Dewey, M.D., Samir Kapadia, M.D., Vasilis Babaliaros, M.D., Vinod H. Thourani, M.D., Paul Corso, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart J. Pocock, Ph.D., for the PARTNER Trial Investigators*

PARTNER 1A

5-Year Follow-Up Presented at ACC 2015

- PARTNER showed that ~35% of patients survived to 5 years, regardless of treatment
- This study provided the first confirmation that TAVR is a reasonable alternative to surgery in high risk patients

[1]Mack, et al., presented at ACC 2015

CoreValve US Pivotal Trial

3-Year Follow-Up Presented at ACC 2016

The CoreValve Pivotal Trial was the first to show a survival advantage with TAVR compared to SAVR, with separation of the all-cause mortality curves maintained to 3 years

[1]Deeb, et al., *J Am Coll Cardiol* 2016 Mar 22; doi: 10.1016/j.jacc.2016.03.506

Guidelines:
TAVR in Patients at Intermediate Surgical Risk

2017 Update, Prior to SURTAVI Data Release

IIa	**B-R**	**TAVR is a reasonable alternative to surgical AVR for symptomatic patients with severe AS (Stage D) and an intermediate surgical risk, depending on patient-specific procedural risks, values, and preferences (62-65).**	**NEW:** New RCT showed noninferiority of TAVR to surgical AVR in symptomatic patients with severe AS at intermediate surgical risk.
See Online Data Supplements 5 and 9 (Updated From 2014 VHD Guideline)			

Nishimura et al. 2017 AHA/ACC Focuesed Update of the 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease. Circulation 2017 Mar 15

Patients at Intermediate Surgical Risk

Trials randomizing intermediate surgical risk patients to TAVR or SAVR

PARTNER IIA Trial

TAVR, N=1011, STS 5.8% vs SAVR, N=1021, STS 5.8%

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael J. Mack, M.D., Raj R. Makkar, M.D., Lars G. Svensson, M.D., Ph.D., Susheel K. Kodali, M.D., Vinod H. Thourani, M.D., E. Murat Tuzcu, M.D., D. Craig Miller, M.D., Howard C. Herrmann, M.D., Darshan Doshi, M.D., David J. Cohen, M.D., Augusto D. Pichard, M.D., Samir Kapadia, M.D., Todd Dewey, M.D., Vasilis Babaliaros, M.D., Wilson Y. Szeto, M.D., Mathew R. Williams, M.D., Dean Kereiakes, M.D., Alan Zajarias, M.D., Kevin L. Greason, M.D., Brian K. Whisenant, M.D., Robert W. Hodson, M.D., Jeffrey W. Moses, M.D., Alfredo Trento, M.D., David L. Brown, M.D., William F. Fearon, M.D., Philippe Pibarot, D.V.M., Ph.D., Rebecca T. Hahn, M.D., Wael A. Jaber, M.D., William N. Anderson, Ph.D., Maria C. Alu, M.M., and John G. Webb, M.D., for the PARTNER 2 Investigators*

CoreValve SURTAVI Trial

TAVR, N=864, STS 4.4% vs SAVR, N=796, STS 4.5%

The NEW ENGLAND JOURNAL of MEDICINE

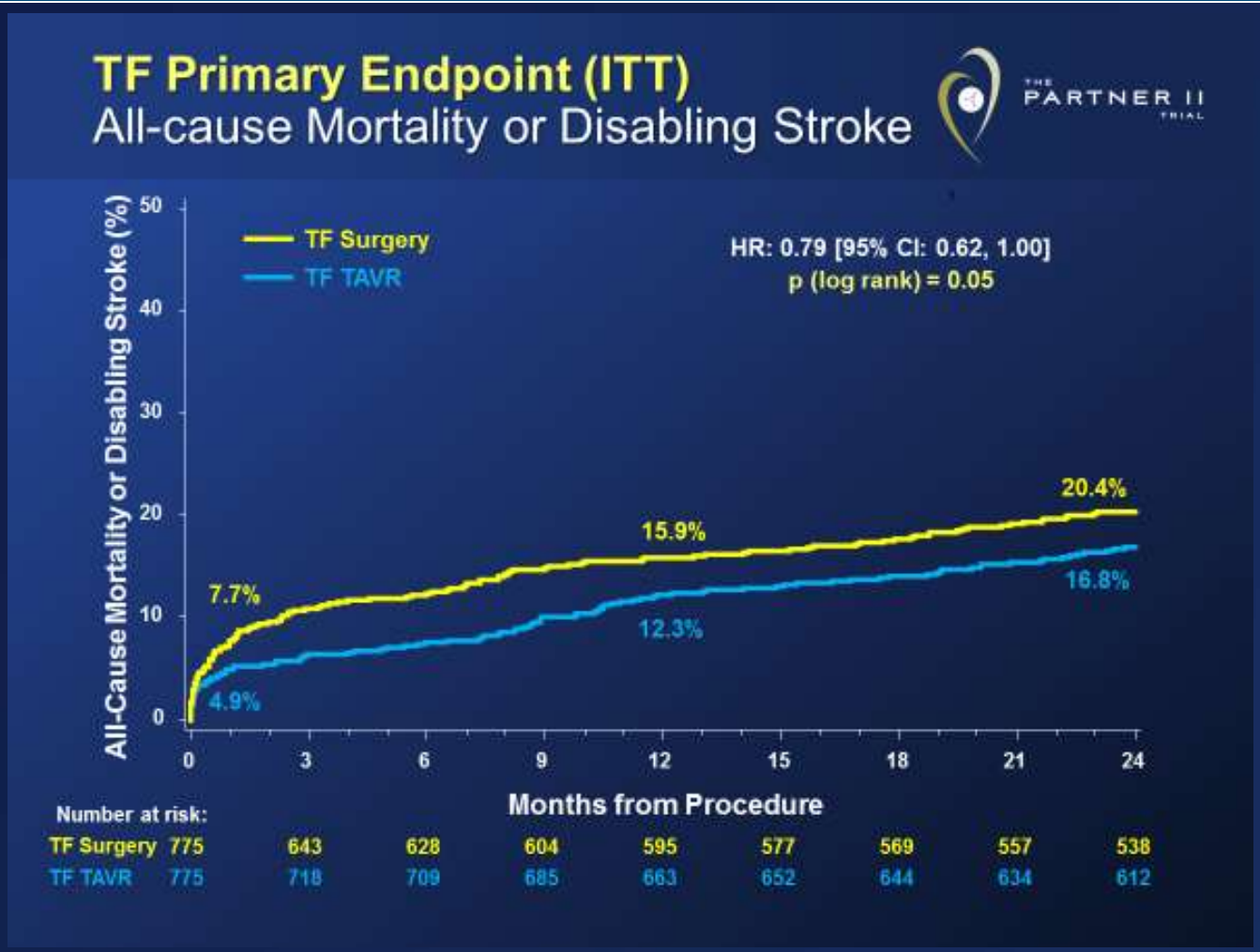
ORIGINAL ARTICLE

Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients

M.J. Reardon, N.M. Van Mieghem, J.J. Popma, N.S. Kleiman, L. Søndergaard, M. Mumtaz, D.H. Adams, G.M. Deeb, B. Maini, H. Gada, S. Chetcuti, T. Gleason, J. Heiser, R. Lange, W. Merhi, J.K. Oh, P.S. Olsen, N. Piazza, M. Williams, S. Windecker, S.J. Yakubov, E. Grube, R. Makkar, J.S. Lee, J. Conte, E. Vang, H. Nguyen, Y. Chang, A.S. Mugglin, P.W.J.C. Serruys, and A.P. Kappetein, for the SURTAVI Investigators*

PARTNER IIA Trial

The results from PARTNER IIA supported the use of TAVR as an alternative to surgery in intermediate risk patients.



Smith et al Presented at ACC 2016

PARTNER IIA Trial

TAVR had significantly reduced life threatening/disabling bleeding, AKI, and New AF, while SAVR had significantly reduced major vascular complications

Other Clinical Endpoints (ITT)
At 30 Days and 2 Years

THE PARTNER II TRIAL

Events (%)	30 Days			2 Years		
	TAVR (n = 1011)	Surgery (n = 1021)	p-value*	TAVR (n = 1011)	Surgery (n = 1021)	p-value*
Rehospitalization	6.5	6.5	0.99	19.6	17.3	0.22
MI	1.2	1.9	0.22	3.6	4.1	0.56
Major Vascular Complications	7.9	5.0	0.008	8.6	5.5	0.006
Life-Threatening / Disabling Bleeding	10.4	43.4	<0.001	17.3	47.0	<0.001
AKI (Stage III)	1.3	3.1	0.006	3.8	6.2	0.02
New Atrial Fibrillation	9.1	26.4	<0.001	11.3	29.3	<0.001
New Permanent Pacemaker	8.5	6.9	0.17	11.8	10.3	0.29
Re-intervention	0.4	0.0	0.05	1.4	0.6	0.09
Endocarditis	0.0	0.0	NA	1.2	0.7	0.22

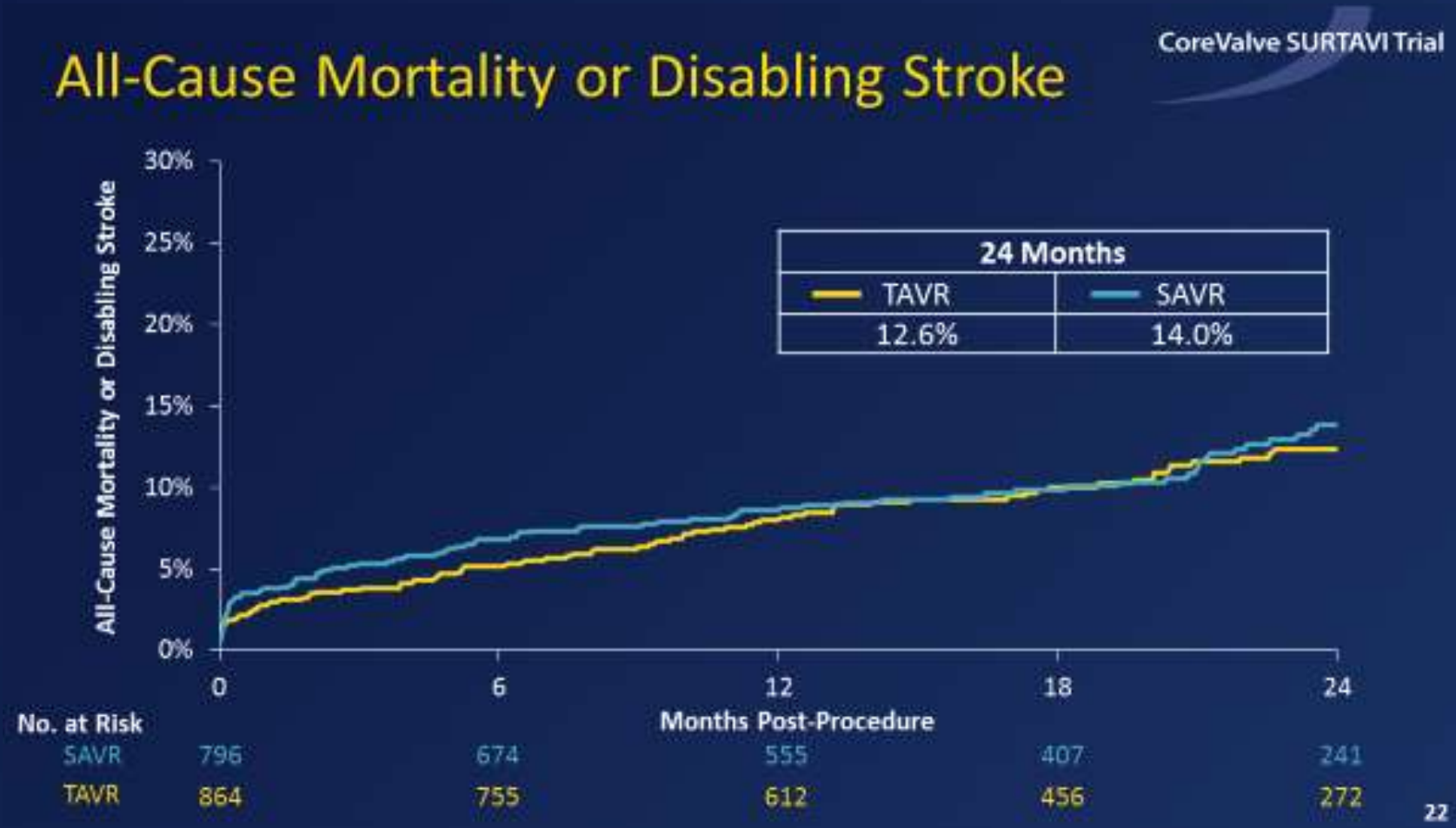
*Event rates are KM estimates, p-values are point in time

Smith et al. Presented at ACC 2016

CoreValve SURTAVI trial

Presented at ACC 2017

The SURTAVI trial demonstrated that TAVR with a self-expanding CoreValve or Evolut R bioprosthesis is noninferior to SAVR for all-cause mortality or disabling stroke at 24 months.



Reardon et al. Presented at ACC 2017

CoreValve SURTAVI trial

TAVR showed significantly less 30 day stroke, AKI, atrial fibrillation and transfusion use while SAVR had less residual aortic regurgitation, major vascular complications and fewer new pacemakers.

30-Day Safety and Procedure-related Complications

	TAVR (N=864)	SAVR (N=796)	95% CI for Difference
All-cause mortality or disabling stroke	2.8	3.9	-2.8, 0.7
All-cause mortality	2.2	1.7	-0.9, 1.8
Disabling stroke	1.2	2.5	-2.6, 0.1
All stroke	3.4	5.6	-4.2, -0.2
Overt life-threatening or major bleeding	12.2	9.3	-0.1, 5.9
Transfusion of PRBCs* - n (%)			
0 units	756 (87.5)	469 (58.9)	24.4, 32.5
2 – 4 units	48 (5.6)	136 (17.1)	-14.5, -8.5
≥ 4 units	31 (3.6)	101 (12.7)	-11.7, -6.5
Acute kidney injury, stage 2-3	1.7	4.4	-4.4, -1.0
Major vascular complication	6.0	1.1	3.2, 6.7
Cardiac perforation	1.7	0.9	-0.2, 2.0
Cardiogenic shock	1.1	3.8	-4.2, -1.1
Permanent pacemaker implant	25.9	6.6	15.9, 22.7
Atrial fibrillation	12.9	43.4	-34.7, -26.4

*Percentage rates, all others are Bayesian rates

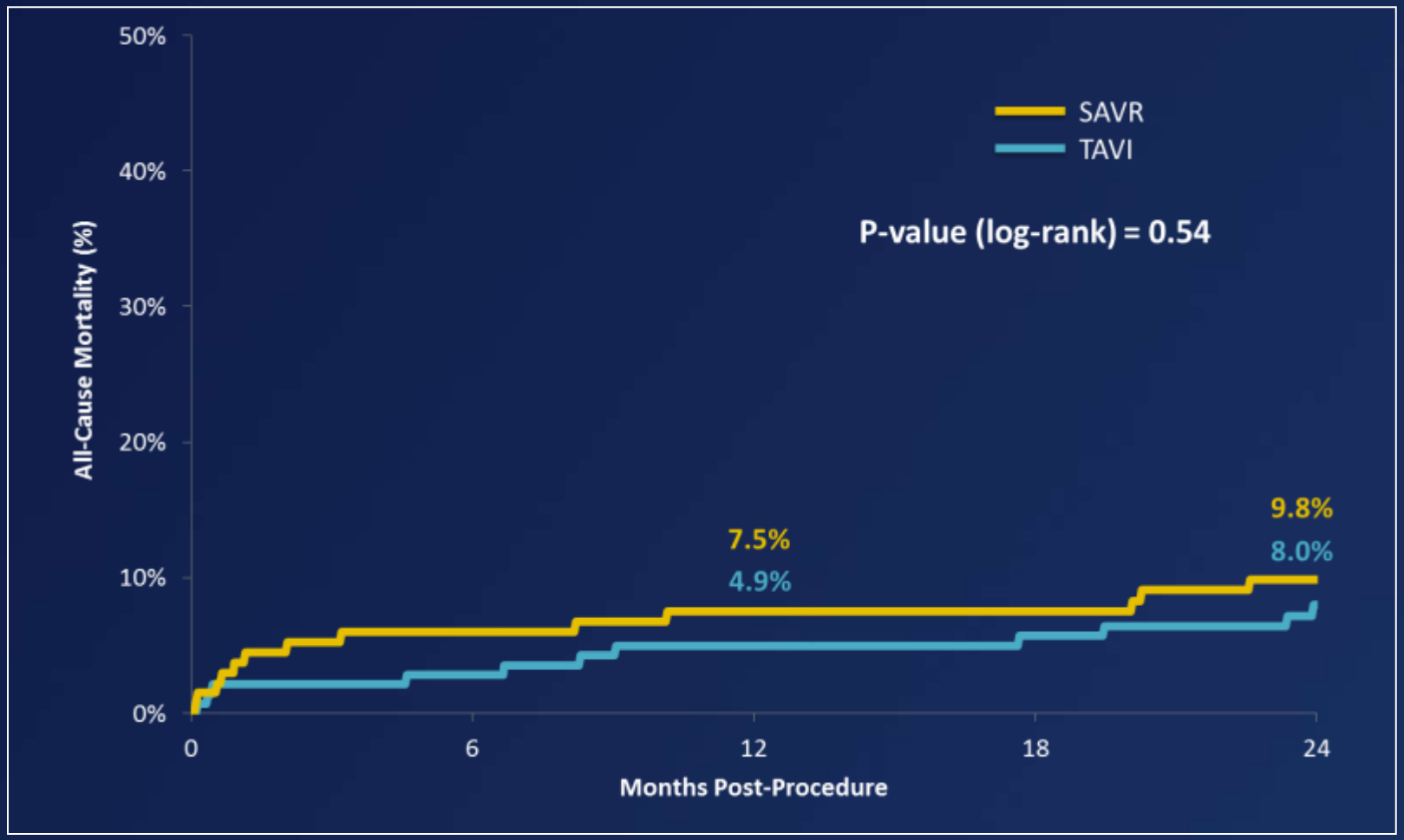
15

Reardon et al. Presented at ACC 2017

Lower surgical Risk

NOTION | The CoreValve Platform

Though the study was likely under-powered, NOTION showed all-cause mortality with TAVR to be non-inferior to SAVR



[1]Sondergaard, presented at EuroPCR 2015

Guidelines: TAVR in Patients at Low Surgical Risk

2014 Guideline

Table 10. Summary of Recommendations for AS: Choice of Surgical or Transcatheter Intervention

Recommendations	COR	LOE	References
Surgical AVR is recommended in patients who meet an indication for AVR (Section 3.2.3) with low or intermediate surgical risk	I	A	(74,148)
For patients in whom TAVR or high-risk surgical AVR is being considered, members of a Heart Valve Team should collaborate to provide optimal patient care	I	C	N/A
TAVR is recommended in patients who meet an indication for AVR for AS who have a prohibitive surgical risk and a predicted post-TAVR survival >12 mo	I	B	(169,170)
TAVR is a reasonable alternative to surgical AVR in patients who meet an indication for AVR (Section 3.2.3) and who have high surgical risk (Section 2.5)	IIa	B	(171,172)
Percutaneous aortic balloon dilation may be considered as a bridge to surgical or transcatheter AVR in severely symptomatic patients with severe AS	IIb	C	N/A
TAVR is not recommended in patients in whom existing comorbidities would preclude the expected benefit from correction of AS	III: No Benefit	B	(169)

AS indicates aortic stenosis; AVR, aortic valve replacement; COR, Class of Recommendation; LOE, Level of Evidence; N/A, not applicable; and TAVR, transcatheter aortic valve replacement.

Nishimura et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the ACC/AHA task force on practice guidelines. J Thorac Cardiovasc Surg. 2014 Jul;148(1):e1-e132

Low Surgical Risk

Active Trials Randomizing TAVR to SAVR

Medtronic Low Risk[1]

N = ~1200

Up to 80 centers
Evolut R, all routes

Industry-sponsored
10-year follow-up

PARTNER 3[2]

N = 1228

Up to 64 centers
SAPIEN 3,
transfemoral

Industry-sponsored
10-year follow-up

UK TAVI[3]

N = 808

All UK TAVI centers
All valves, all routes

Publically funded
5-year follow-up

NOTION-2[4]

N = 992

All Nordic countries
All valves,
transfemoral

Physician and
industry-sponsored
5-year follow-up

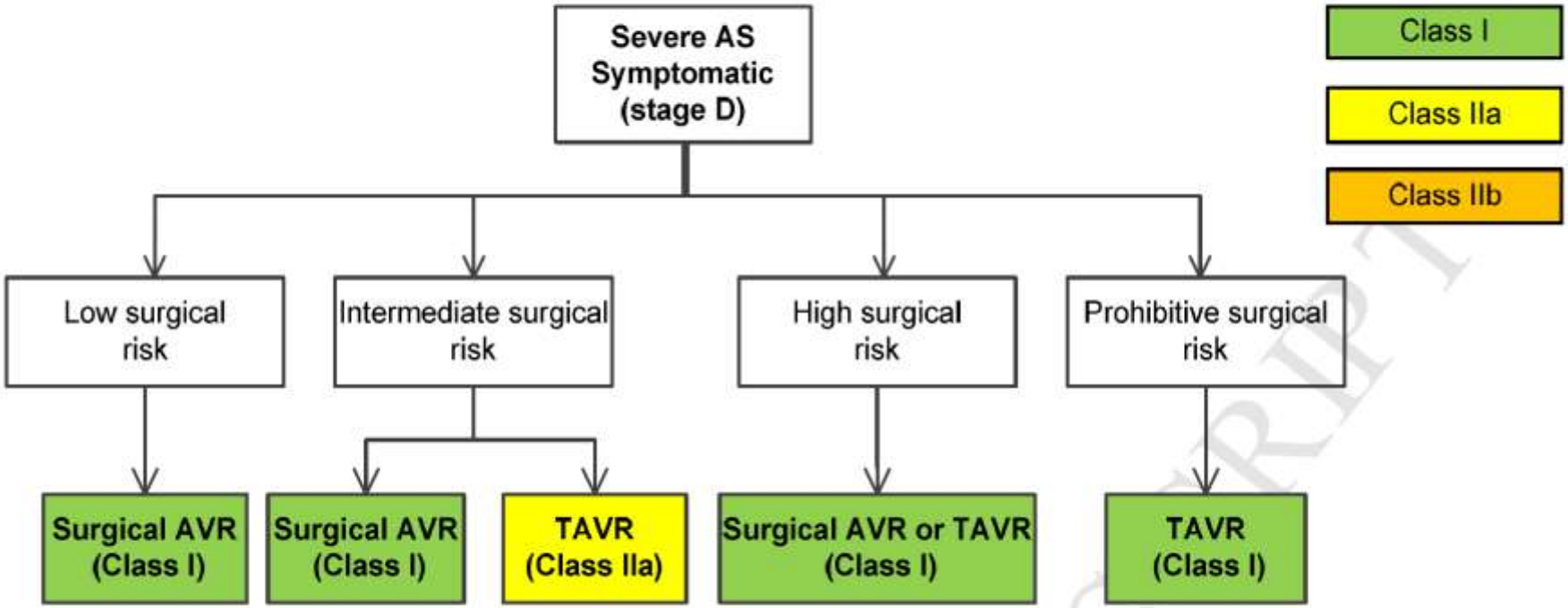
[1]Popma, et al., presented at TCT 2016; [2]Mack, et al., presented at TCT 2016; [3]Moat, et al., presented at TCT 2016; [4]Sondergaard, et al., presented at TCT 2016

TAVR and SAVR Treatment for Severe Symptomatic Aortic Stenosis

2017 Update

Nishimura, et al.
2017 VHD Focused Update

Figure 1. Choice of TAVR Versus Surgical AVR in the Patient With Severe Symptomatic AS



AS indicates aortic stenosis; AVR, aortic valve replacement; and TAVR, transcatheter aortic valve replacement.

Nishimura et al. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease. Circulation 2017 Mar 15

Feasibility in Common Anatomic Variations

TAVR Guidelines: Bicuspid Aortic Valve Patients

2014 Guideline. Limited indications on TAVR and bicuspid valves

CLASS I

1. TTE is indicated in patients with signs or symptoms of AS or a bicuspid aortic valve for accurate diagnosis of the cause of AS, hemodynamic severity, LV size, and systolic function, and for determining prognosis and timing of valve intervention (24,25,89). *(Level of Evidence: B)*

CLASS I

1. Operative intervention to repair the aortic sinuses or replace the ascending aorta is indicated in patients with a bicuspid aortic valve if the diameter of the aortic sinuses or ascending aorta is greater than 5.5 cm (113,267,268). *(Level of Evidence: B)*

CLASS IIa

1. Operative intervention to repair the aortic sinuses or replace the ascending aorta is reasonable in patients with bicuspid aortic valves if the diameter of the aortic sinuses or ascending aorta is greater than 5.0 cm and a risk factor for dissection is present (family history of aortic dissection or if the rate of increase in diameter is ≥0.5 cm per year). *(Level of Evidence: C)*

Nishimura et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the ACC/AHA task force on practice guidelines. J Thorac Cardiovasc Surg. 2014 Jul;148(1):e1-e132

Future Studies: Bicuspid Aortic Valve Patients

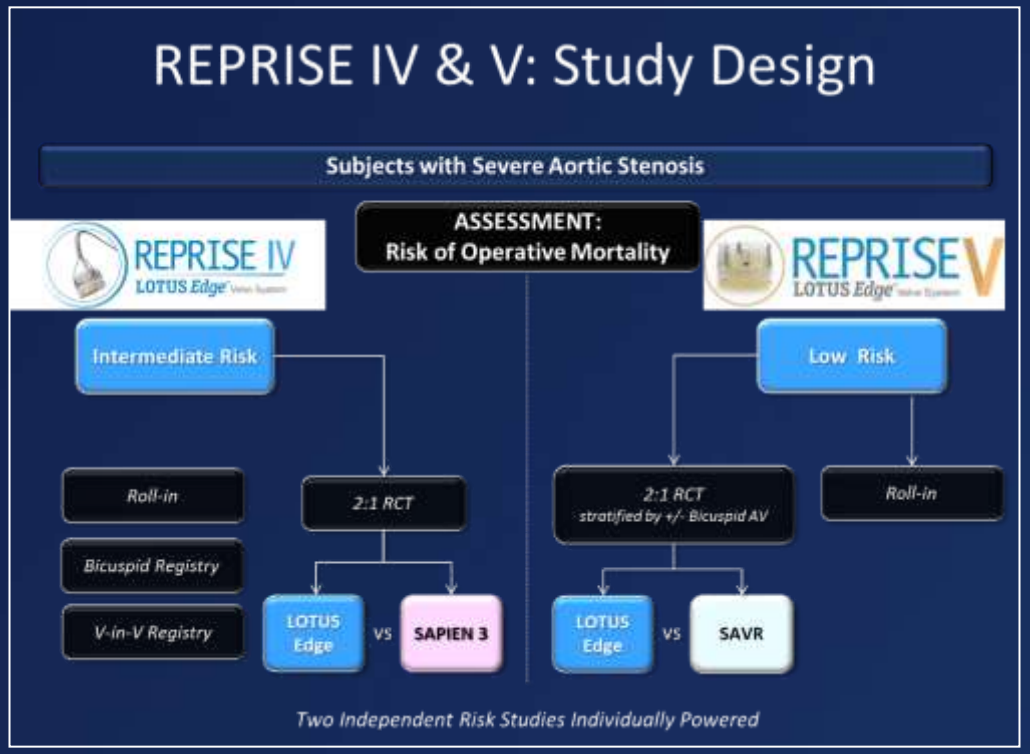
PARTNER 3 Low risk trial is including arm with bicuspid aortic valve patients

Lotus REPRISE V low risk trial including arm with bicuspid aortic valve patients

Low risk Trials
SAVR - TAVR

Partner 3

- STS score <4; no age restriction; no bicuspid valves; N=1228
- Risk < 3%; no Syntaxscore >22; no bicuspid valve; N=1256
- Heart team agrees on Low risk; with bicuspid valves
- STS <=4, age <=75 years; N=992



Kappetein, presented at ACC 2017

Earlier Intervention

Guidelines: Asymptomatic Severe Aortic Stenosis Patients

2014 Guidelines

Table 9. Summary of Recommendations for AS: Timing of Intervention

Recommendations	COR	LOE	References
AVR is recommended for symptomatic patients with severe high-gradient AS who have symptoms by history or on exercise testing (stage D1)	I	B	(9,91,134,135)
AVR is recommended for asymptomatic patients with severe AS (stage C2) and LVEF <50%	I	B	(136,137)
AVR is indicated for patients with severe AS (stage C or D) when undergoing other cardiac surgery	I	B	(108,138)
AVR is reasonable for asymptomatic patients with very severe AS (stage C1, aortic velocity ≥5.0 m/s) and low surgical risk	IIa	B	(139,140)
AVR is reasonable in asymptomatic patients (stage C1) with severe AS and decreased exercise tolerance or an exercise fall in BP	IIa	B	(25,47)
AVR is reasonable in symptomatic patients with low-flow/low-gradient severe AS with reduced LVEF (stage D2) with a low-dose dobutamine stress study that shows an aortic velocity ≥4.0 m/s (or mean pressure gradient ≥40 mm Hg) with a valve area ≤1.0 cm^2 at any dobutamine dose	IIa	B	(43,141,142)
AVR is reasonable in symptomatic patients who have low-flow/low-gradient severe AS (stage D3) who are normotensive and have an LVEF ≥50% if clinical, hemodynamic, and anatomic data support valve obstruction as the most likely cause of symptoms	IIa	C	N/A
AVR is reasonable for patients with moderate AS (stage B) (aortic velocity 3.0–3.9 m/s) who are undergoing other cardiac surgery	IIa	C	N/A
AVR may be considered for asymptomatic patients with severe AS (stage C1) and rapid disease progression and low surgical risk	IIb	C	N/A

AS indicates aortic stenosis; AVR, aortic valve replacement by either surgical or transcatheter approach; BP, blood pressure; COR, Class of Recommendation; LOE, Level of Evidence; LVEF, left ventricular ejection fraction; and N/A, not applicable.

Nishimura et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the ACC/AHA task force on practice guidelines. J Thorac Cardiovasc Surg. 2014 Jul;148(1):e1-e132

Future Studies:
A Randomized Trial in Asymptomatic Patients

The AVATAR (Aortic Valve Replacement versus Conservative Treatment in Asymptomatic Severe Aortic Stenosis Trial) study has begun in Europe. AVATAR is a randomized multicenter controlled randomizing patients to surgical aortic valve replacement or conventional drug treatment

Journal of the American College of Cardiology

Volume 67, Issue 16, April 2016
DOI: 10.1016/j.jacc.2016.01.068

A Randomized Trial in Patients With Asymptomatic Severe Aortic Stenosis
A Future Has Begun!
Marko Banovic, Serge D. Nikolic, Svetozar Putnik

Banovic et al. A randomized trial in patients with asymptomatic severe aortic stenosis. JACC vol 67, issue 16, April 2016

SAPIEN 3 Study on Asymptomatic Patients

Edwards has initiated a prospective, randomized, multicenter study randomizing asymptomatic aortic stenosis patients to TAVR with SAPIEN 3 or clinical surveillance

Anticipated start date: April 2017

Evaluation of Transcatheter Aortic Valve Replacement Compared to SurveilLance for Patients With AsYmptomatic Severe Aortic Stenosis (EARLY TAVR)

This study is not yet open for participant recruitment. (see Contacts and Locations)

Verified February 2017 by Edwards Lifesciences

Sponsor:
Edwards Lifesciences

Information provided by (Responsible Party):
Edwards Lifesciences

ClinicalTrials.gov Identifier:
NCT03042104

First received: January 30, 2017
Last updated: February 3, 2017
Last verified: February 2017
History of Changes

ClinicalTrials.Gov

Guideline: Moderate AS

2014 Guideline

Table 9. Summary of Recommendations for AS: Timing of Intervention

Recommendations	COR	LOE	References
AVR is recommended for symptomatic patients with severe high-gradient AS who have symptoms by history or on exercise testing (stage D1)	I	B	(9,91,134,135)
AVR is recommended for asymptomatic patients with severe AS (stage C2) and LVEF <50%	I	B	(136,137)
AVR is indicated for patients with severe AS (stage C or D) when undergoing other cardiac surgery	I	B	(108,138)
AVR is reasonable for asymptomatic patients with very severe AS (stage C1, aortic velocity ≥5.0 m/s) and low surgical risk	IIa	B	(139,140)
AVR is reasonable in asymptomatic patients (stage C1) with severe AS and decreased exercise tolerance or an exercise fall in BP	IIa	B	(25,47)
AVR is reasonable in symptomatic patients with low-flow/low-gradient severe AS with reduced LVEF (stage D2) with a low-dose dobutamine stress study that shows an aortic velocity ≥4.0 m/s (or mean pressure gradient ≥40 mm Hg) with a valve area ≤1.0 cm^2 at any dobutamine dose	IIa	B	(43,141,142)
AVR is reasonable in symptomatic patients who have low-flow/low-gradient severe AS (stage D3) who are normotensive and have an LVEF ≥50% if clinical, hemodynamic, and anatomic data support valve obstruction as the most likely cause of symptoms	IIa	C	N/A
AVR is reasonable for patients with moderate AS (stage B) (aortic velocity 3.0–3.9 m/s) who are undergoing other cardiac surgery	IIa	C	N/A
AVR may be considered for asymptomatic patients with severe AS (stage C1) and rapid disease progression and low surgical risk	IIb	C	N/A

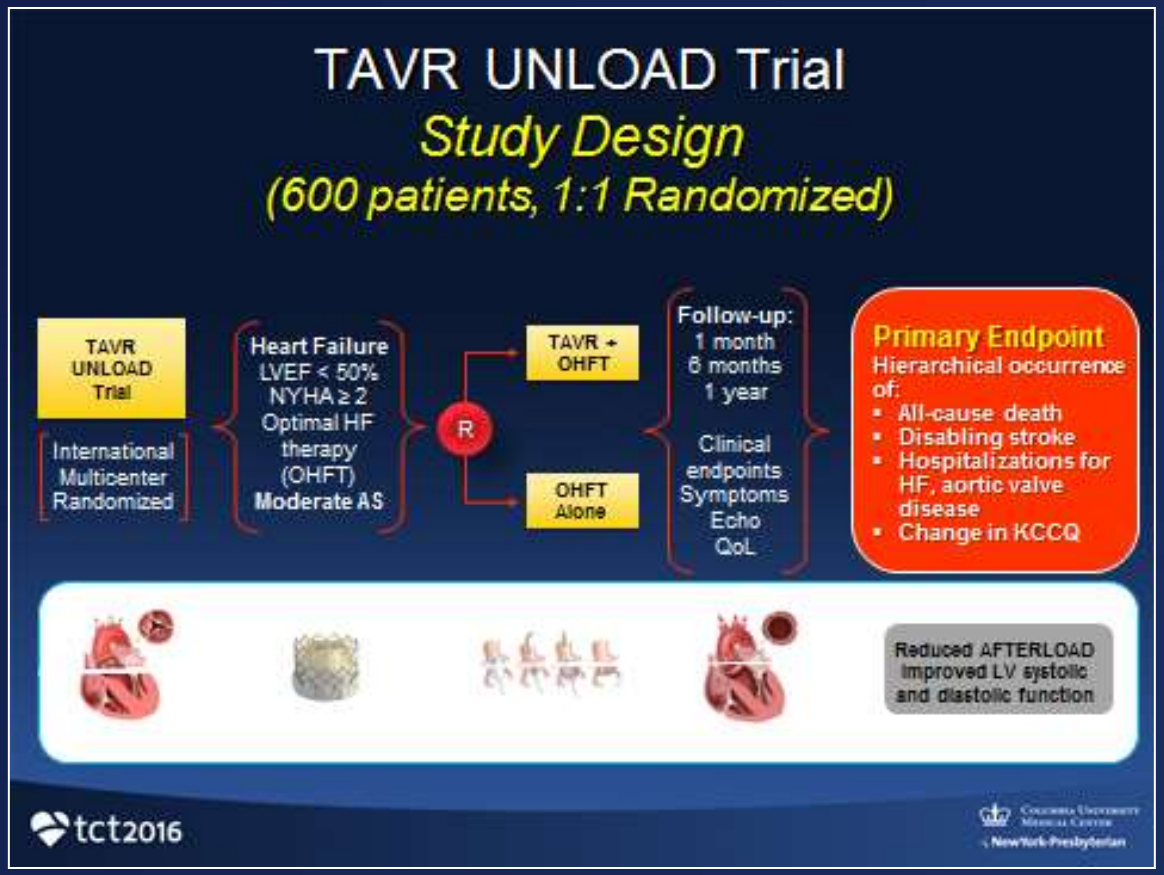
AS indicates aortic stenosis; AVR, aortic valve replacement by either surgical or transcatheter approach; BP, blood pressure; COR, Class of Recommendation; LOE, Level of Evidence; LVEF, left ventricular ejection fraction; and N/A, not applicable.

Nishimura et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the ACC/AHA task force on practice guidelines. J Thorac Cardiovasc Surg. 2014 Jul;148(1):e1-e132

Moderate Aortic Stenosis and Reduced Ejection Fraction

TAVR UNLOAD Trial (NCT02661451)

- TAVR UNLOAD is a multicenter, randomized trial comparing TAVR with SAPIEN 3 in addition to optimal heart failure therapy vs. optimal therapy alone in patients with moderate aortic stenosis
- This study will show whether early TAVR in patients with moderate AS, symptoms of heart failure, and reduced EF will be superior to current strategies of watchful waiting and medical therapy



[1]Spitzer, et al., *Am Heart J* 2016; 182:80-88; [2]Leon, et al., presented at TCT 2016

Final Thoughts

- TAVR is now proven in patients at intermediate surgical risk, which represents the culmination of many years of rigorous study.
- Currently there is significant clinical investment in applying this technology to younger patients at low surgical risk.
- Careful study is an absolute requirement because certain TAVR-specific complications remain a concern.
- However, the survival advantage and quick recovery to improved quality of life which was achieved with transfemoral TAVR versus SAVR in the high risk and intermediate risk trials provides a highly encouraging signal.

Thank you for your kind Attention