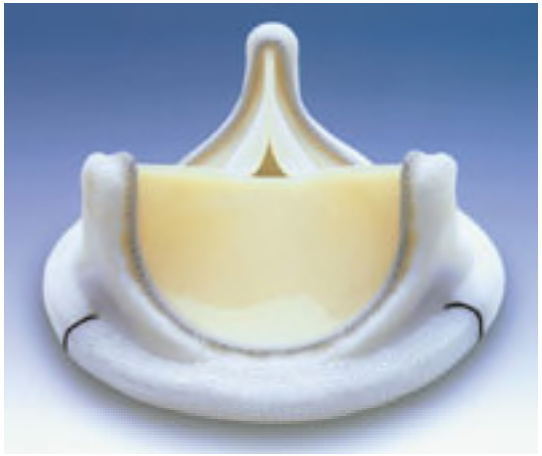


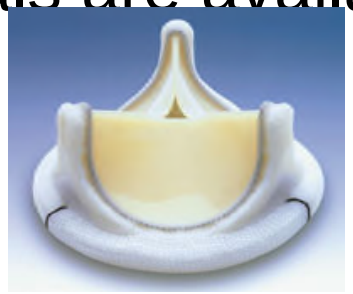
Endocarditis in Patients with severe aortic stenosis treated with either surgical or transcatheter bioprosthesis, longterm follow up from the NOTION study

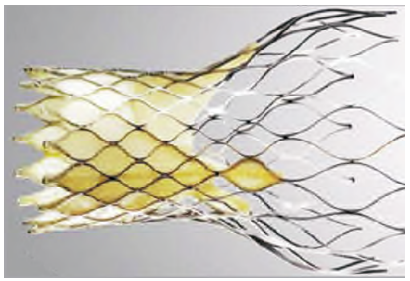
Nikolaj Ihlemann MD, Phd
Rigshospitalet, Cardiology Department, University Hospital of Copenhagen

- No disclosures

Background

- TAVI is currently recognised as being equally effective as surgical bioprosthesis in patients with intermediate or high surgical risk
- Concerns has been raised on the durability of transcatheter valves and longterm data are currently sparse
- Valve durability and complications also includes *prosthesis endocarditis* and few longterm data from the randomized trials are available





Prosthesis IE in the RCT

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*

ABSTRACT

BACKGROUND

Previous trials have shown that among high-risk patients with aortic stenosis, survival rates are similar with transcatheter aortic-valve replacement (TAVR) and surgical aortic-valve replacement. We evaluated the two procedures in a randomized trial involving

RESULTS

The rate of death from any cause or disabling stroke was similar in the TAVR group and the surgery group (P=0.001 for noninferiority). At 2 years, the Kaplan–Meier event rates were 19.3% in the TAVR group and 21.1% in the surgery group (hazard ratio in the TAVR group, 0.89; 95% confidence interval [CI], 0.73 to 1.09; P=0.25). In the transfemoral-access cohort, TAVR resulted in a lower rate of death or disabling stroke than surgery (hazard ratio, 0.79; 95% CI, 0.62 to 1.00; P=0.05), whereas in the transthoracic-access cohort, outcomes were similar in the two groups. TAVR resulted in larger aortic-valve areas than did surgery and also resulted in lower rates of acute kidney injury, severe bleeding, and new-onset atrial fibrillation; surgery resulted in fewer major vascular complications and less paravalvular aortic regurgitation.

CONCLUSIONS

In intermediate-risk patients, TAVR was similar to surgical aortic-valve replacement with respect to the primary end point of death or disabling stroke. (Funded by Edwards Lifesciences; PARTNER 2 ClinicalTrials.gov number, NCT01314313.)

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr Leon at Columbia University Medical Center, 161 Ft. Washington Ave., 6th Floor, or at mleon@crf.org

published on April 2, 2016

PARTNER 2 IE at 2 year:
1.2% vs 0.7%
TAVI vs SAVR

The NEW ENGLAND JOURNAL of MEDICINE

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*

ABSTRACT

BACKGROUND

We compared transcatheter aortic-valve replacement (TAVR), using a self-expanding transcatheter aortic-valve bioprosthesis, with surgical aortic-valve replacement in patients with severe aortic stenosis and an increased risk of death during surgery.

METHODS

We recruited patients with severe aortic stenosis who were at increased surgical risk

cantly lower in the TAVR group than in the surgical group (14.2% vs. 19.1%), with an absolute reduction in risk of 4.9 percentage points (upper boundary of the 95% confidence interval, −0.4; P<0.001 for noninferiority; P = 0.04 for superiority). The results were similar in the intention-to-treat analysis. In a hierarchical testing procedure, TAVR was noninferior with respect to echocardiographic indexes of valve stenosis, functional status, and quality of life. Exploratory analyses suggested a reduction in the rate of major adverse cardiovascular and cerebrovascular events and no increase in the risk of stroke.

CONCLUSIONS

In patients with severe aortic stenosis who are at increased surgical risk, TAVR with a self-expanding transcatheter aortic-valve bioprosthesis was associated with a significantly higher rate of survival at 1 year than surgical aortic-valve replacement. (Funded by Medtronic; U.S. CoreValve High Risk Study ClinicalTrials.gov number, NCT01240902.)

From Mount Sinai Medical Center, New York (D.H.A.), and St. Francis Hospital, Roslyn (N.R., G.P.) — both in New York; Beth Israel Deaconess Medical Center, Boston (J.J.P.); Houston Methodist DeBakey Heart and Vascular Center (M.J.R., N.S.K.), and Texas Heart Institute at St. Luke's Medical Center (J.S.C.) — both in

Pinnacle Health, Harrisburg, PA (B.M., M.M.); and Medtronic, Minneapolis (S. Chenoweth), and Mayo Clinical Foundation, Rochester (J.K.O.) — both in Minnesota. Address reprint requests to Dr. Popma at Interventional Cardiology Service, Beth Israel Deaconess Medical Center, 185 Pilgrim Rd., Boston, MA 02460, or at jpopma@bidmc.harvard.edu.

*A complete list of the investigators, institutions, and research organizations participating in the U.S. CoreValve High Risk Study is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on March 29, 2014, at NEJM.org.

US corevalve trial at 3 year:
0.9% vs 1.7%
TAVI vs SAVR

Prosthesis (TAVI) IE in registries

JAMA | Original Investigation

Association Between Transcatheter Aortic Valve Replacement and Subsequent Infective Endocarditis and In-Hospital Death

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IMPORTANCE Limited data exist on clinical characteristics and outcomes of patients who had infective endocarditis after undergoing transcatheter aortic valve replacement (TAVR).

OBJECTIVE To determine the associated factors, clinical characteristics, and outcomes of patients who had infective endocarditis after TAVR.

DESIGN, SETTING, AND PARTICIPANTS The Infectious Endocarditis after TAVR International Registry included patients with definite infective endocarditis after TAVR from 47 centers from Europe, North America, and South America between June 2005 and October 2015.

EXPOSURE Transcatheter aortic valve replacement for incidence of infective endocarditis and infective endocarditis for in-hospital mortality.

MAIN OUTCOMES AND MEASURES Infective endocarditis and in-hospital mortality after infective endocarditis.

RESULTS A total of 250 cases of infective endocarditis occurred in 20 006 patients after TAVR (incidence, 1.1% per person-year; 95% CI, 1.1%-1.4%; median age, 80 years; 64% men). Median time from TAVR [IQR], 1.5-13.4 months). The cl tive endocarditis after TAVR was per year; 95% CI, 0.94-0.99), ma nellitus (41.7% vs 30.0%; HR, 1.52; 95% CI, 1.02-2.29), and moderate to severe aortic regurgitation (22.4% vs 14.7%; HR, 2.05; 95% CI, 1.28-3.28). Health care-associated infective endocarditis was present in 52.8% (95% CI, 46.6%-59.0%) of patients. *Enterococci* species and *Staphylococcus aureus* were the most frequently isolated microorganisms (24.6%; 95% CI, 19.1%-30.1% and 23.3%; 95% CI, 17.9%-28.7%, respectively). The in-hospital mortality rate was 36% (95% CI, 30.0%-41.9%; 90 deaths; 160 survivors), and surgery was performed in 14.8% (95% CI, 10.4%-19.2%) of patients during the infective endocarditis episode. In-hospital mortality was associated with a higher logistic EuroSCORE (23.1% vs 18.6%; odds ratio [OR], 1.03 per 1% increase; 95% CI, 1.00-1.05), heart failure (59.3% vs 23.7%; OR, 3.36; 95% CI, 1.74-6.45), and acute kidney injury (67.4% vs 31.6%; OR, 2.70; 95% CI, 1.42-5.11). The 2-year mortality rate was 66.7% (95% CI, 59.0%-74.2%; 132 deaths; 115 survivors).

CONCLUSIONS AND RELEVANCE Among patients undergoing TAVR, younger age, male sex, history of diabetes mellitus, and moderate to severe residual aortic regurgitation were significantly associated with an increased risk of infective endocarditis. Patients who developed endocarditis had high rates of in-hospital mortality and 2-year mortality.

1.1% per year

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Supplemental content

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Structural Heart Disease

Prosthetic Valve Endocarditis After Transcatheter Aortic Valve Implantation

Niels Thue Olsen, MD, PhD; Ole De Backer, MD, PhD; Hans G.H. Thyregod, MD; Niels Vejlstrup, MD; Henning Bundgaard, MD, DMSc; Lars Søndergaard, MD, DMSc; Nikolaj Ihlemann, MD, PhD

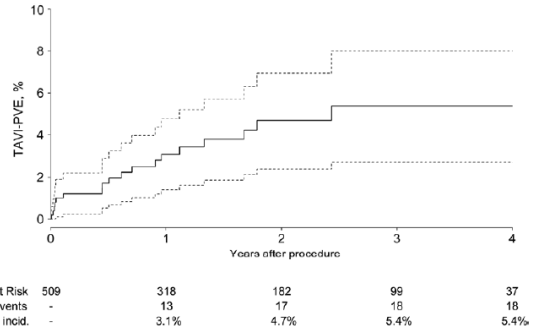
Background—Transcatheter aortic valve implantation (TAVI) is an advancing mode of treatment for inoperable or high-risk patients with aortic stenosis. Prosthetic valve endocarditis (PVE) after TAVI is a serious complication, but only limited data exist on its incidence, outcome, and procedural risk factors.

Methods and Results—Observational single-center study of 509 consecutive patients treated with a transcatheter implanted self-expandable aortic valve prosthesis (Medtronic CoreValve). We identified 18 patients diagnosed with TAVI-PVE during a median follow-up pe gest follow-up was 6.3 years). TAVI-PVE was most frequent in th [confidence interval, 1.4%–4.8%]); the overall annualized rate w %). Seventeen patients (94%) were treated conservatively and 1 ditis or complications to treatment, 2 of those (11%) during initial hospitalization for PVE. An increased risk of TAVI-PVE was seen in patients with low implanted valve position (hazard ratio, 2.8 [1.1–7.2]), moderate or worse postprocedural paravalvular regurgitation (hazard ratio, 4.0 [1.5–11]), implantation of >1 prosthesis (hazard ratio, 5.2 [1.5–18]), and any vascular complication (hazard ratio, 3.8 [1.5–9.8]).

Conclusions—TAVI-PVE occurred at a slightly higher rate than reported for surgically implanted valves. Conservative treatment was associated with an acceptable outcome. Suboptimal valve deployment and vascular complications were associated with an increased risk of TAVI-PVE. (*Circ Cardiovasc Interv*. 2015;8:e001939. DOI: 10.1161/CIRCINTERVENTIONS.114.001939.)

3.1% first year

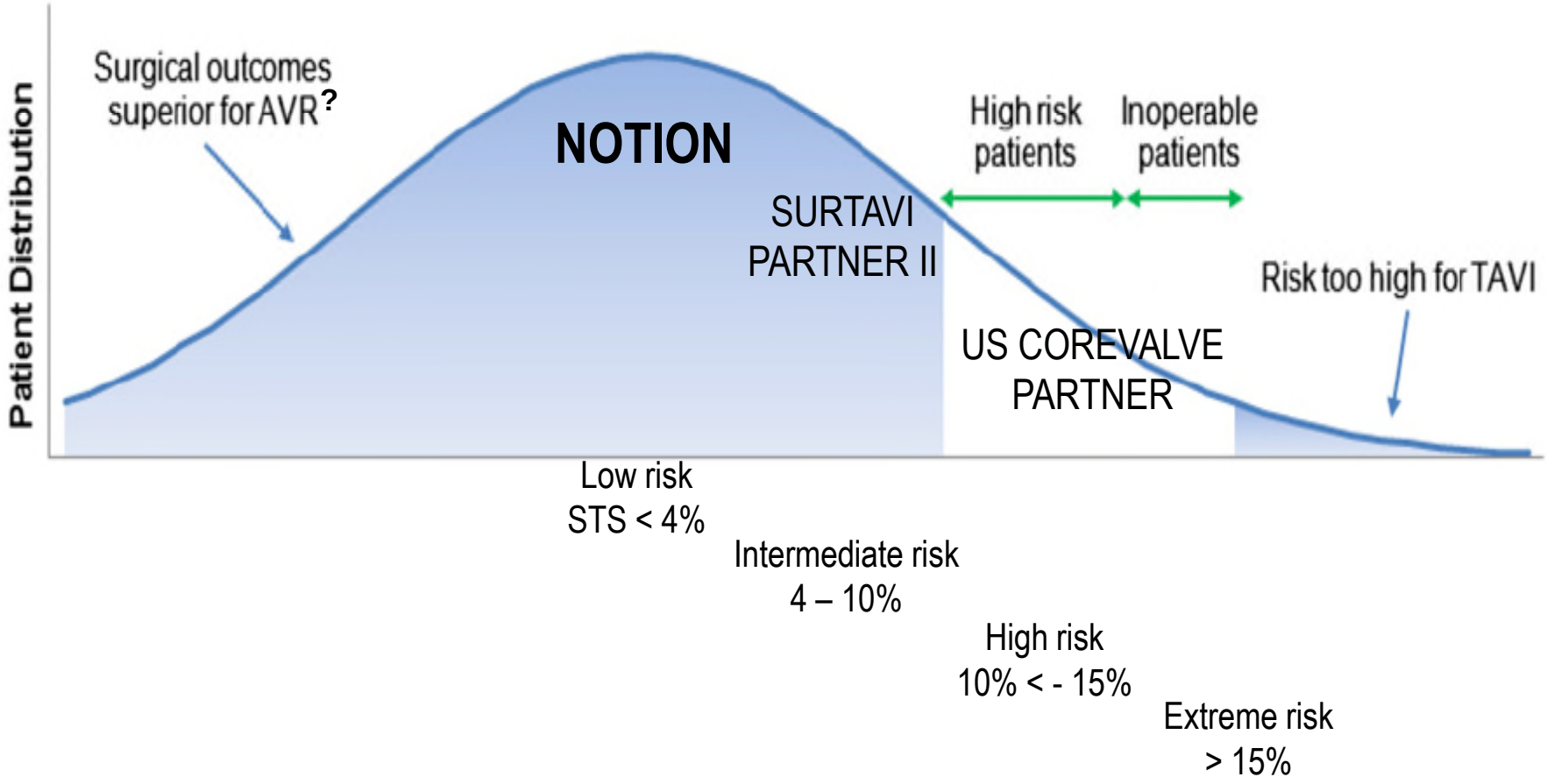
Key Words: endocarditis ■ transcatheter aortic valve replacement



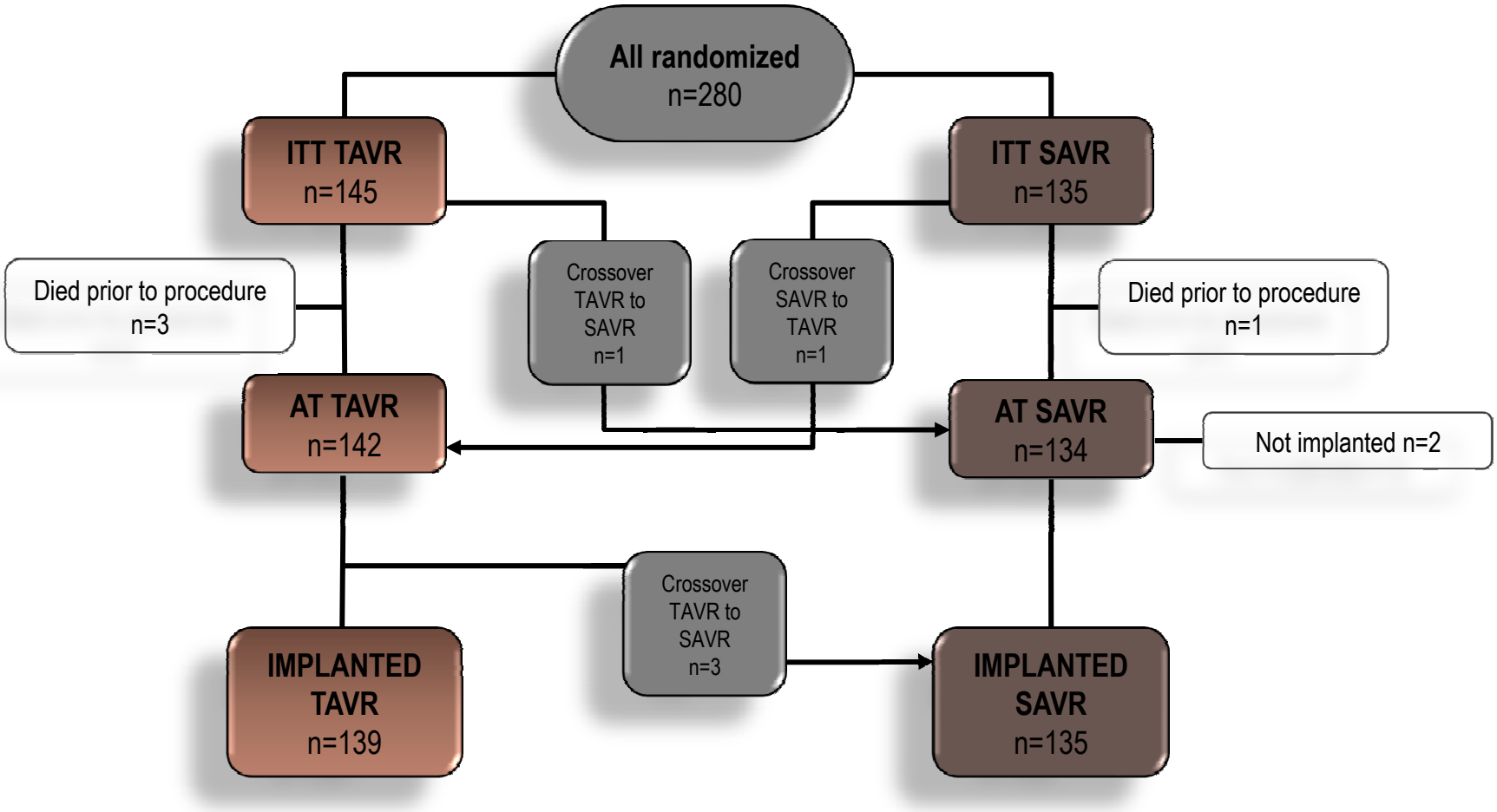
Nordic Aortic Valve Intervention (NOTION) Trial

Objective:	Compare TAVR vs. SAVR in patients ≥ 70 years eligible for surgery (all-comers population)
Primary outcome:	Composite rate of death from any cause, stroke or myocardial infarction at 1 year (VARC II-defined)
Secondary outcomes:	Safety and efficacy (NYHA), echocardiographic outcomes (VARC II-defined)
Design:	Prospective, multicenter, non-blinded, randomized trial
Enrollment period:	December 2009 - April 2013

Operative Risk and TAVR vs. SAVR Trials



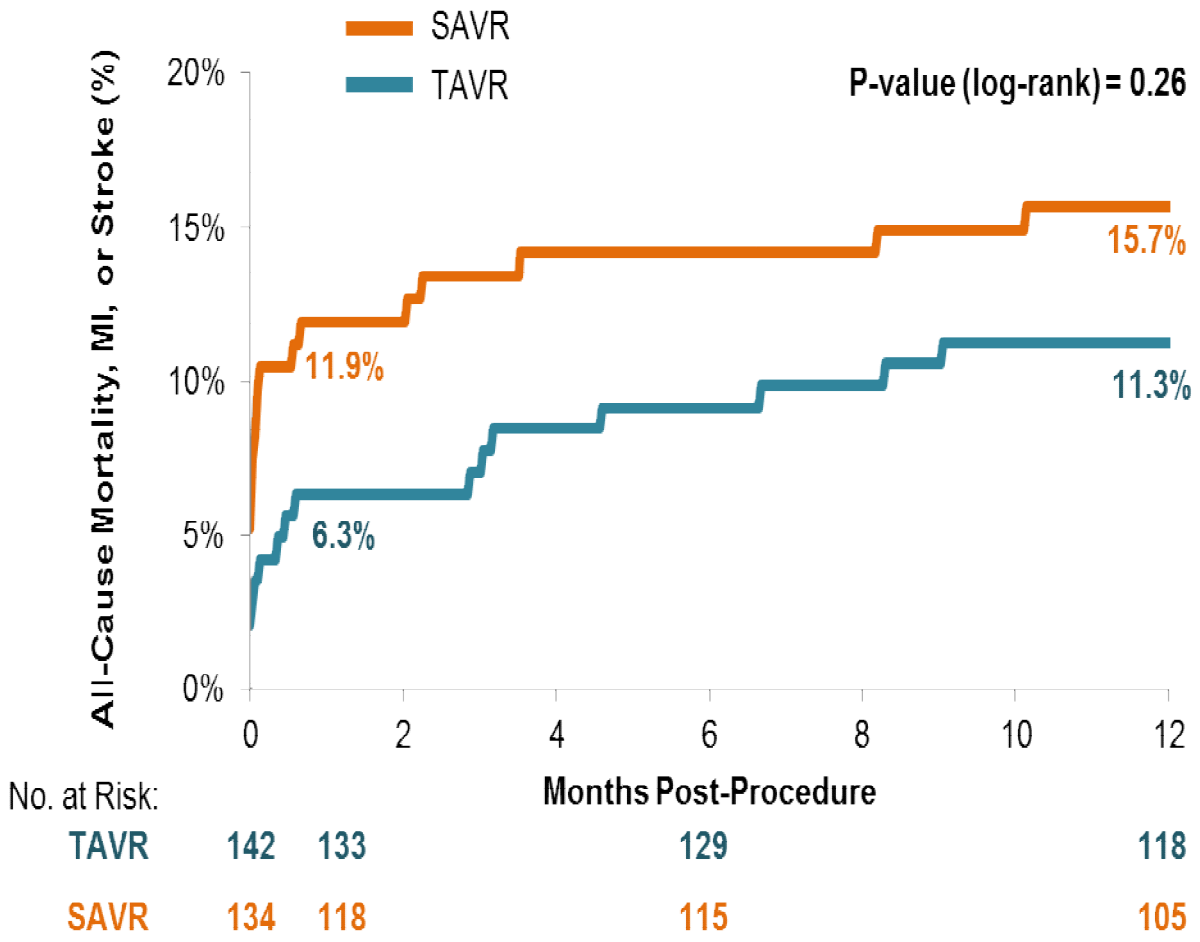
Trial Flow


All randomized
n=280
ITT TAVR
n=145
ITT SAVR
n=135
Died prior to procedure
n=3
Crossover
TAVR to
SAVR
n=1
Crossover
SAVR to
TAVR
n=1
Died prior to procedure
n=1
AT TAVR
n=142
AT SAVR
n=134
Not implanted n=2
Crossover
TAVR to
SAVR
n=3
IMPLANTED
TAVR
n=139
IMPLANTED
SAVR
n=135

Baseline Characteristics

Characteristic, % or mean ± SD	TAVR n=145	SAVR n=135	p-value
Age (yrs)	**79.2 ± 4.9**	**79.0 ± 4.7**	0.71
Male	53.8	52.6	0.84
Society of Thoracic Surgeons (STS) Score	**2.9 ± 1.6**	**3.1 ± 1.7**	0.30
STS Score < 4%	83.4	80.0	0.46
Logistic EuroSCORE I	8.4 ± 4.0	8.9 ± 5.5	0.38
NYHA class III or IV	48.6	45.5	0.61

Death from Any Cause, Stroke or Myocardial Infarction at 1 Year in *As-Treated Population*



Possible or *definite* IE

Table 11 Modified Duke criteria for the diagnosis of infective endocarditis (adapted from Li *et al.*[94])

MAJOR CRITERIA

Blood cultures positive for IE:

- Typical microorganisms consistent with IE from two separate blood cultures:
  Viridans streptococci, *Streptococcus bovis*, HACEK group, *Staphylococcus aureus*; or
  Community-acquired enterococci, in the absence of a primary focus;

or

- Microorganisms consistent with IE from persistently positive blood cultures:
  At least two positive blood cultures of blood samples drawn > 12 h apart; or
  All of three or a majority of ≥ 4 separate cultures of blood (with first and last sample drawn at least 1 h apart)

or

- Single positive blood culture for *Coxiella burnetii* or phase I IgG antibody titer > 1 : 800

Evidence of endocardial involvement

- Echocardiography positive for IE
  Vegetation - Abscess - New partial dehiscence of prost
- New valvular regurgitation

- Predisposition: predisposing heart condition, injection d
- Fever: temperature > 38°C
- Vascular phenomena: major arterial emboli, septic pulm
  haemorrhages, Janeway lesions
- Immunologic phenomena: glomerulonephritis, Osler's no
- Microbiological evidence: positive blood culture but does not meet a major criterion or serological evidence of active infection with organism consistent with IE

Diagnosis of IE is definite in the presence of
2 major criteria, or
1 major and 3 minor criteria, or
5 minor criteria

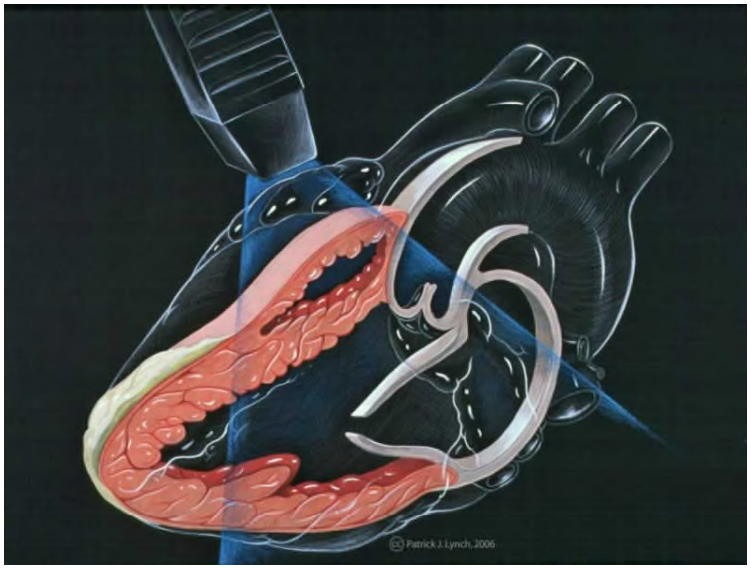
Diagnosis of IE is possible in the presence of
1 major and 1 minor criteria, or
3 minor criteria

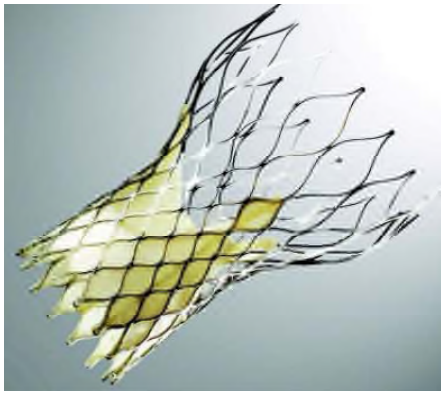
Adapted from Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG, Jr., Ryan T, Bashore T, Corey GR. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis* 2000;**30**:633–638.

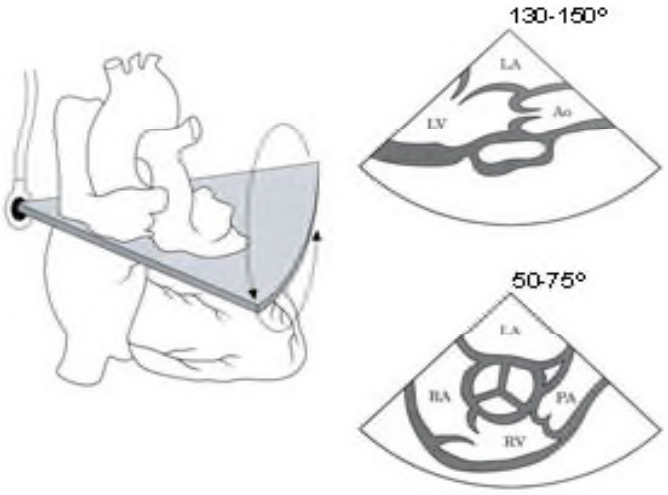
All pt with a prosthetic valve has possible IE when bacteremia is present!

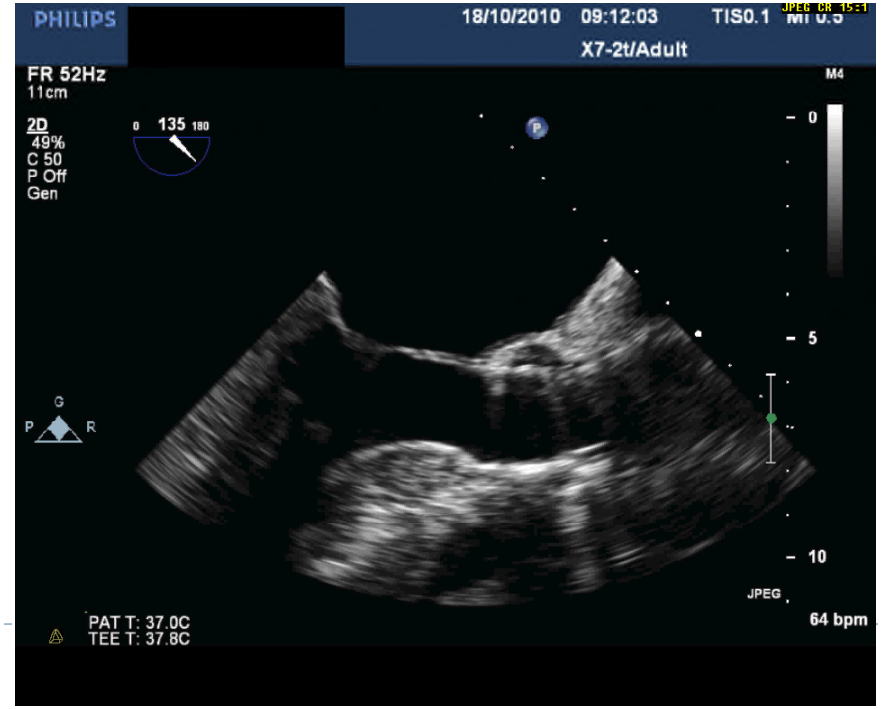
	Possible IE	Definite IE	Total
TAVI	7	9 (7)	**16 (14)**
SAVR	1	7 (9)	**8 (10)**
Total	**8**	**16**	**24**

Diagnostic challenges, shadowing artefacts



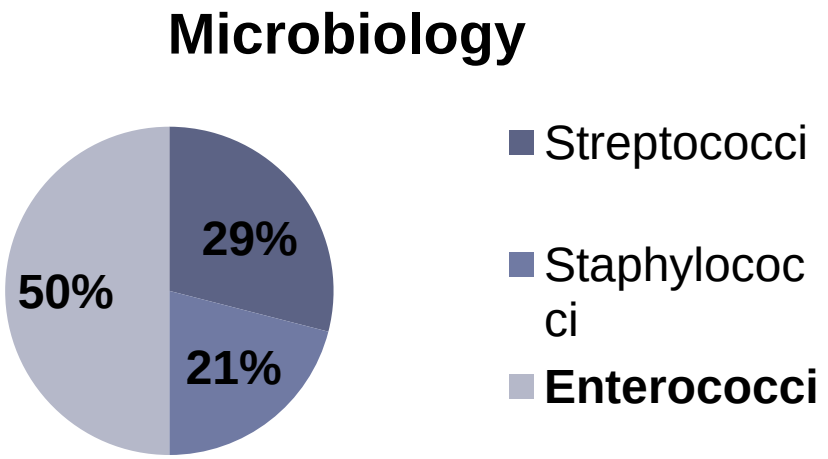




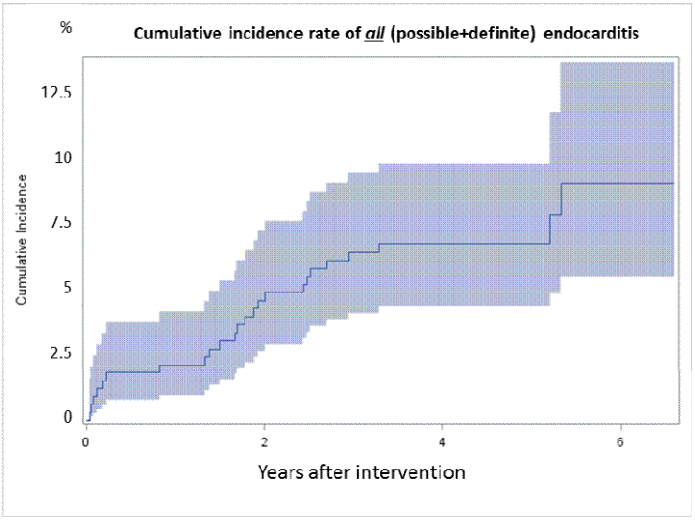


Results

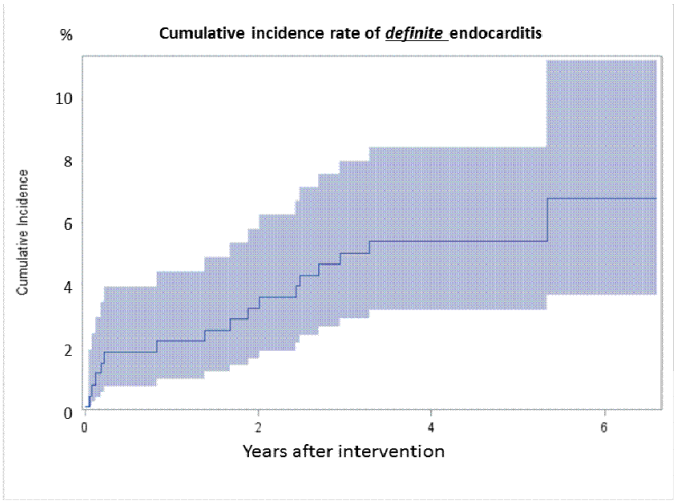
- Follow up time of median 4.1 years (3.7;5.1) year. Maximum of 6.6 years
- Time from procedure to IE: median 626 (244;909) from 14 to 1920 days
- 3 cases of early IE < 30 days: 1 Enterococci, 2 streptococci



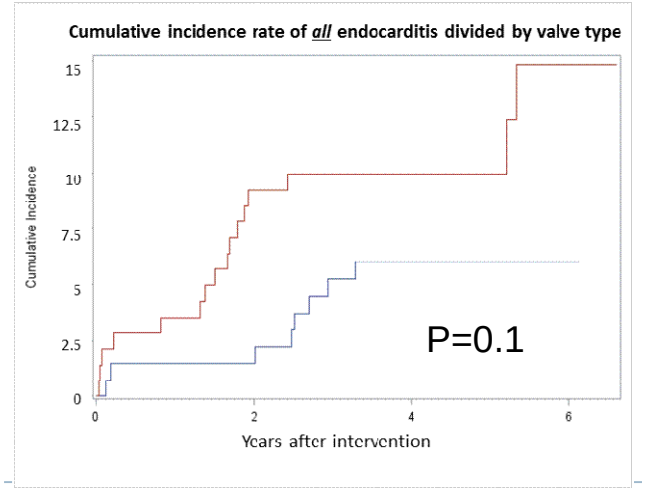
Cumulative incidence *all IE* and *definite IE*

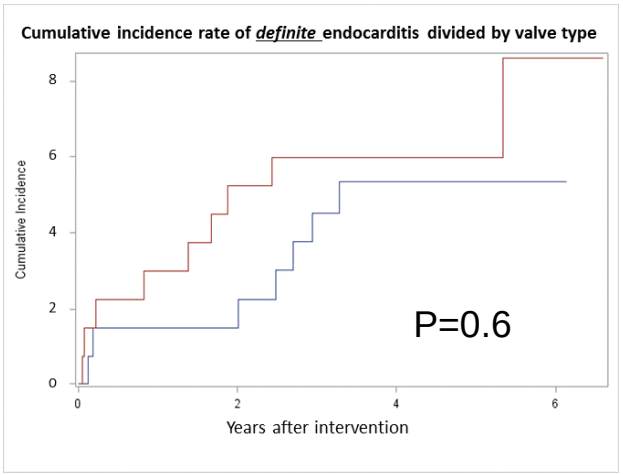


No. at risk	275	238	183	29
No. events	-	15	22	24
Cum. incid.	-	5.2%	7.8%	10.3%

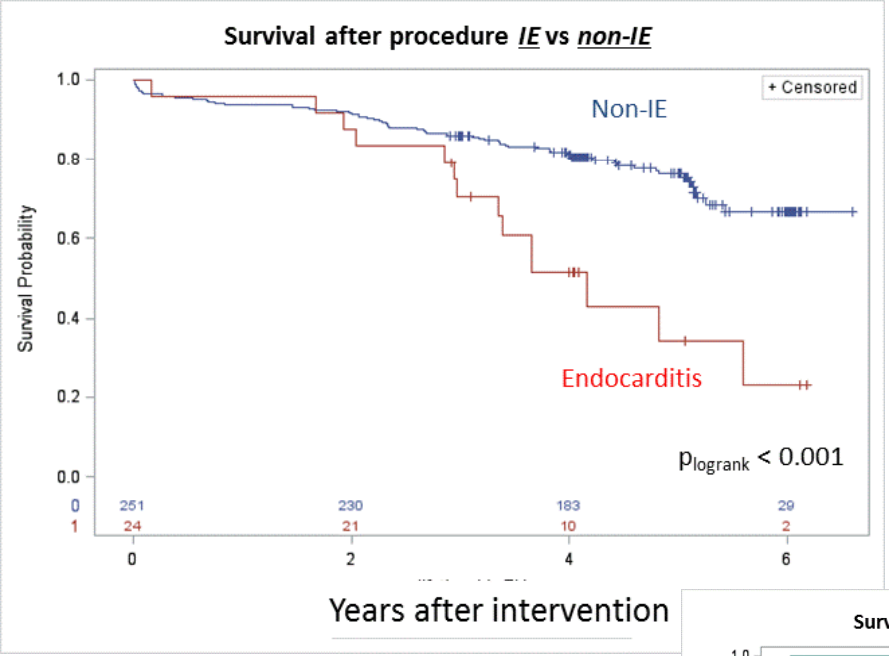


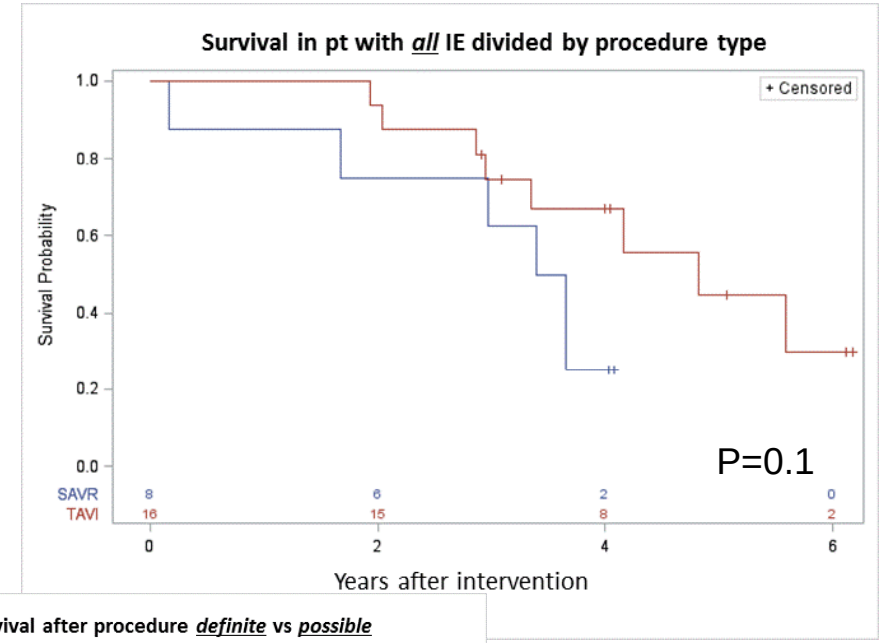
No. at risk	275	238	183	29
No. events	-	9	15	16
Cum. incid.	-	3.2%	5.3%	6.8%

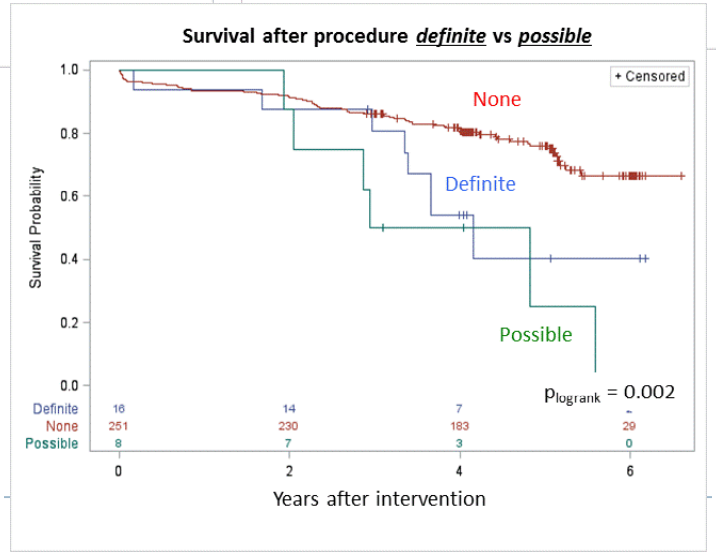




Mortality


Survival after procedure IE vs non-IE
+ Censored
Non-IE
Endocarditis
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
0 251 230 183 29
1 24 21 10 2
0 2 4 6
Years after intervention


Survival in pt with all IE divided by procedure type
+ Censored
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
P=0.1
SAVR 8 6 2 0
TAVI 16 15 8 2
0 2 4 6
Years after intervention


Survival after procedure definite vs possible
+ Censored
None
Definite
Possible
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
Definite 16 14 7
None 251 230 183 29
Possible 8 7 3 0
0 2 4 6
Years after intervention

Risk factors

Logistic regression, univariate

	Odds ratio	P-value
Age	1.05 (0.96-1.15)	0.27
Gender (male)	**2.84 (1.09-7.39)**	**0.03**
Diabetes	0.87 (0.28-2.68)	0.81
STS score	0.52 (0.20-1.36)	0.19
Creatinine	0.81 (0.31-2.13)	0.67
AR	1.22 (0.61-2.42)	0.57
LVEF	1.12 (0.42-2.93)	0.83
Ao mean gradient	1.06 (0.97-1.17)	0.20
PM pre+procedural	1.63 (0.64-4.14)	0.30

Conclusions

- Longest FU of a RCT of TAVI vs SAVR reporting prosthesis endocarditis
- Incidence comparable with previous reports
- No effect of valve type on incidence or mortality
- Enterococci most prevalent bacteriology
- Male gender only detectable risk factors in this study
- Mortality of Prosthetic IE is high
- Incidence difficult to reduce since most cases appear late and are due to endogenous Enterococci bacteremia

Thank you for your attention!

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