TAVR in Low Risk Patients – The 5-year Data

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Disclosures

- Research Valve Trial Participation
  - Edwards Lifesciences
  - Abbott
  - Medtronic

- Course Faculty
  - Edwards Lifesciences

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement for Inoperable Severe Aortic Stenosis

Raj R. Makkar, M.D., Gregory P. Fontana, M.D., Hasan Jilaihawi, M.D., Samir Kapadia, M.D., Augusto D. Pichard, M.D., Pamela S. Douglas, M.D., Vinod H. Thourani, M.D., Vasilis C. Babaliaros, M.D., John G. Webb, M.D., Howard C. Herrmann, M.D., Joseph E. Bavaria, M.D., Susheel Kodali, M.D., David L. Brown, M.D., Bruce Bowers, M.D., Todd M. Dewey, M.D., Lars G. Svensson, M.D., Ph.D., Murat Tuzcu, M.D., Jeffrey W. Moses, M.D., Matthew R. Williams, M.D., Robert J. Siegel, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Stuart Pocock, Ph.D., Craig R. Smith, M.D., and Martin B. Leon, M.D., for the PARTNER Trial Investigators*

ABSTRACT

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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*

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Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients

M.J. Mack, M.B. Leon, V.H. Thourani, R. Makkar, S.K. Kodali, M. Russo, S.R. Kapadia, S.C. Malaisrie, D.J. Col P. Pibarot, J. Leipsic, R.T. Hahn, P. Blanke, M.R. Williams, J.M. McCabe, D.L. Brown, V. Babaliaros, S. Goldm W.Y. Szeto, P. Genereux, A. Pershad, S.J. Pocock, M.C. Alu, J.G. Webb, and C.R. Smith, for the PARTNER 3 Investigators*

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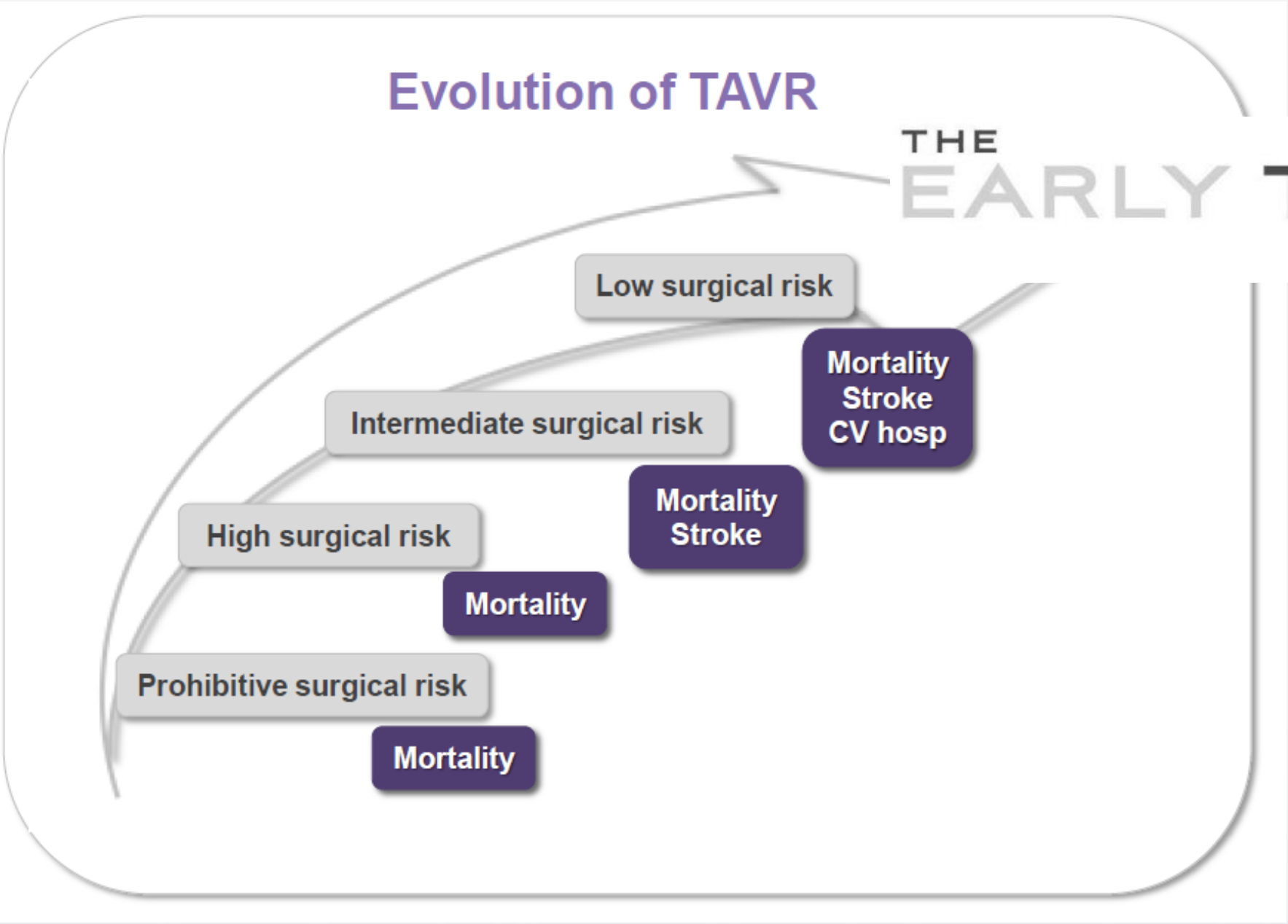
Transcatheter versus Surgical Aortic-Valve Replacement in High-Risk Patients

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*

Evolution of TAVR



Courtesy of Robert Bonow, MD

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

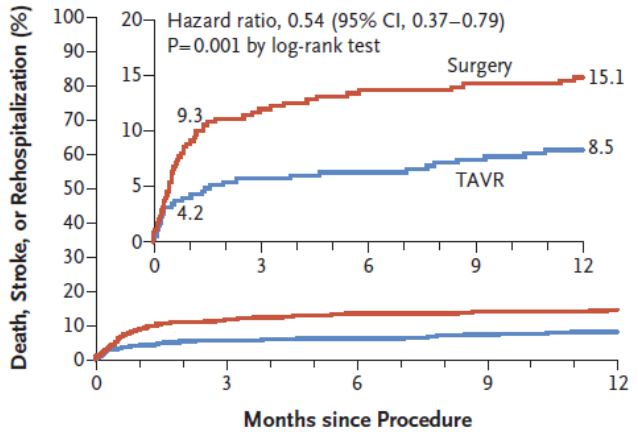
Transcatheter Aortic-Valve Replacement in Low-Risk Patients at Five Years

M.J. Mack, M.B. Leon, V.H. Thourani, P. Pibarot, R.T. Hahn, P. Genereux, S.K. Kodali, S.R. Kapadia, D.J. Cohen, S.J. Pocock, M. Lu, R. White, M. Szerlip, J. Ternacle, S.C. Malaisrie, H.C. Herrmann, W.Y. Szeto, M.J. Russo, V. Babaliaros, C.R. Smith, P. Blanke, J.G. Webb, and R. Makkar, for the PARTNER 3 Investigators*

2023;389:1949-60

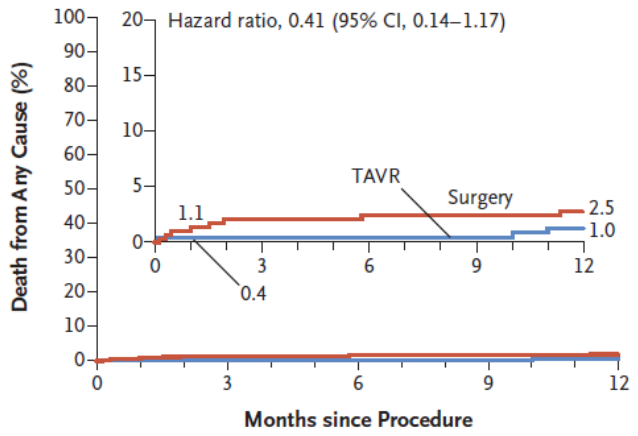
The NEW ENGLAND JOURNAL of MEDICINE

Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients



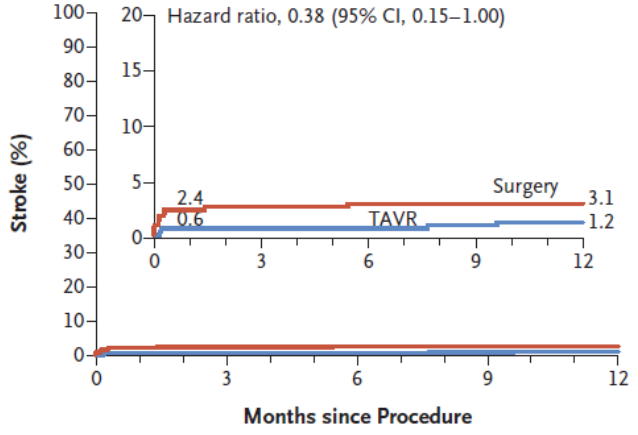
No. at Risk

Surgery	454	408	390	381	377	374
TAVR	496	475	467	462	456	451



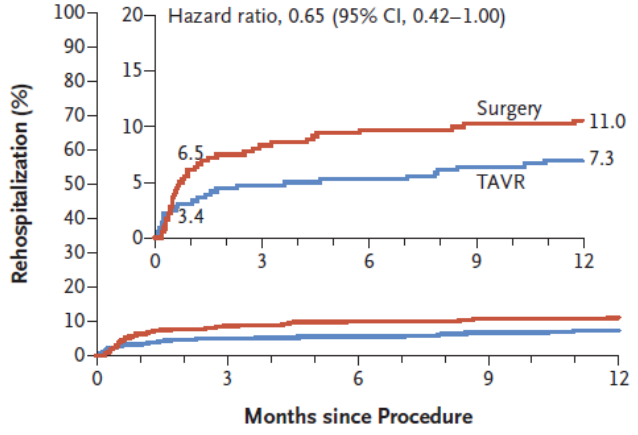
No. at Risk

Surgery	454	445	438	433	431	427
TAVR	496	494	494	493	492	488



No. at Risk

Surgery	454	435	427	423	421	417
TAVR	496	491	491	489	487	484



No. at Risk

Surgery	454	416	399	389	385	382
TAVR	496	477	469	465	459	453

2019;380:1695-705

1000 patients randomized at 71 sites

- 503 underwent TAVR (with SAPIEN 3)
- 497 underwent SAVR

- Mean age 73 years
- 67.5% (TAVR) and 71.1% (SAVR) male
- 92.3% (TAVR) and 90.1% (SAVR) white

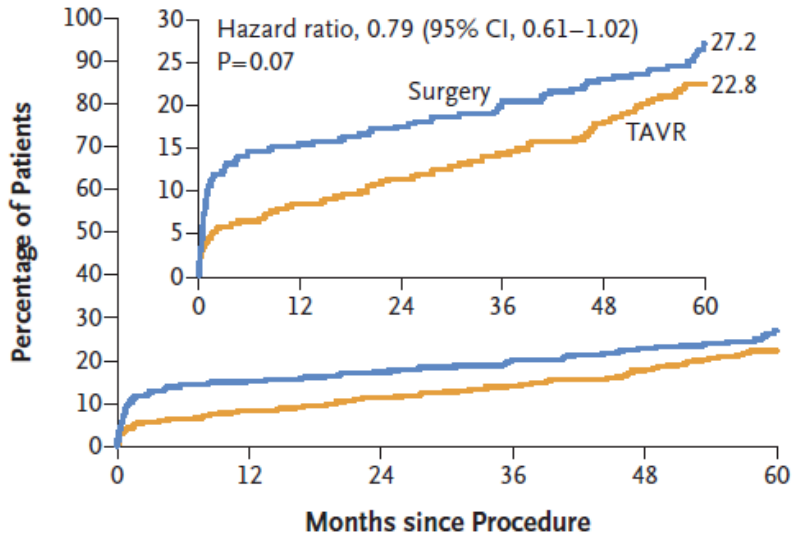
- Mean STS score 1.9%

The 5-year Data

- 1st primary endpoint
  - Death, stroke or rehospitalization (Kaplan-Meier estimates)
- 2nd primary endpoint
  - Death, disabling stroke, nondisabling stroke and # of re-hospitalization days (win ratio analysis)

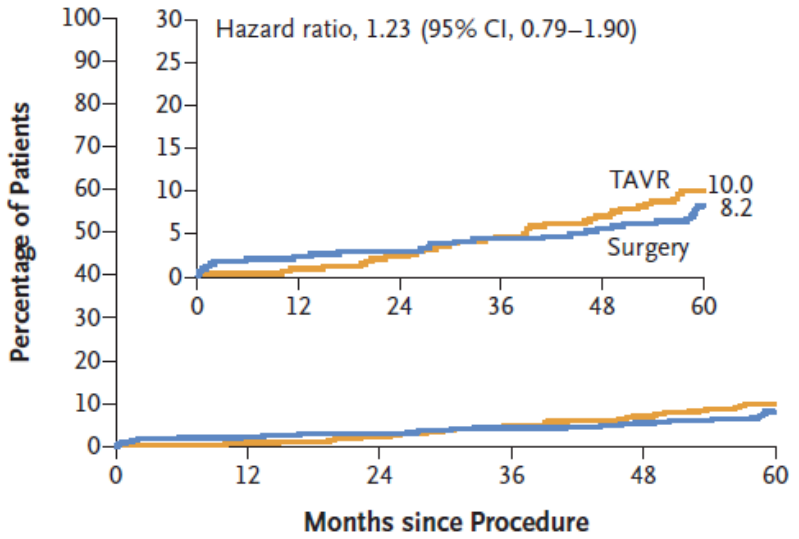
- 22.8% TAVR vs. 27.2% SAVR
  (95% CI -9.9 to 1.3, p=0.07)
- Win ratio for TAVR 1.17
  (95% CI 0.90 to 1.51, p=0.25)

Death from Any Cause, Stroke, or Rehospitalization



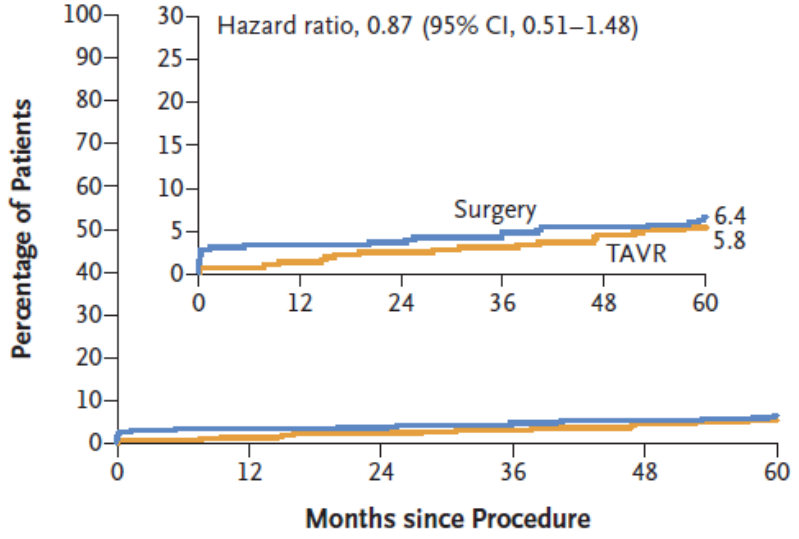
No. at Risk						
Surgery	454	372	349	328	309	276
TAVR	496	453	434	415	391	353

Death from Any Cause



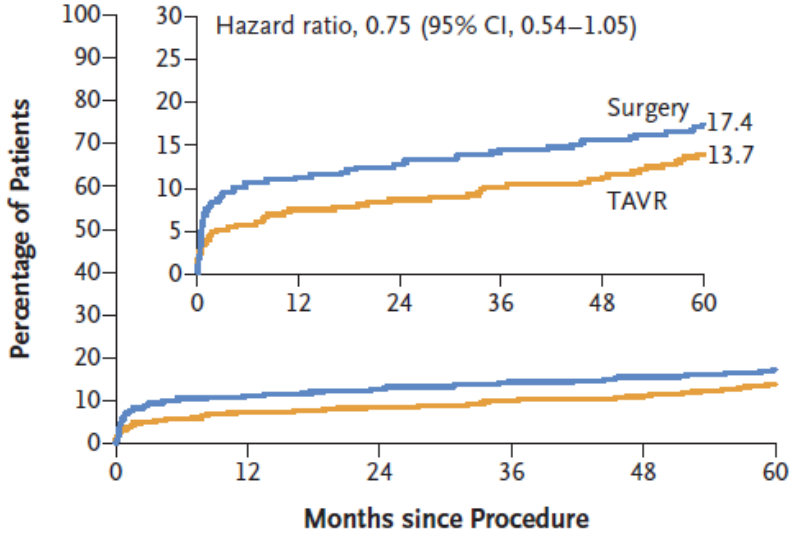
No. at Risk						
Surgery	454	427	409	394	379	346
TAVR	496	490	478	460	438	405

Stroke



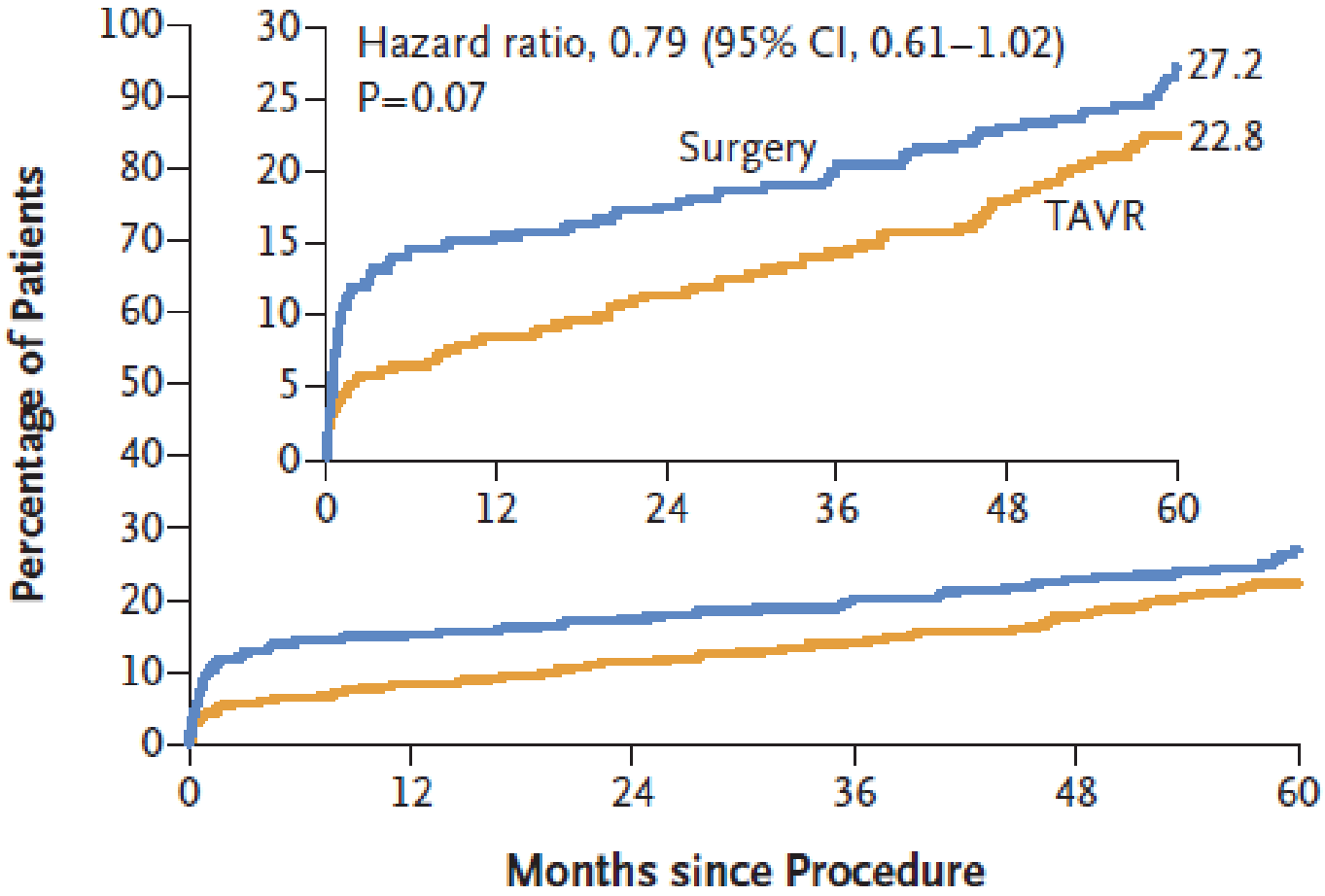
No. at Risk						
Surgery	454	416	397	378	361	329
TAVR	496	486	468	450	428	391

Rehospitalization



No. at Risk						
Surgery	454	381	359	339	321	289
TAVR	496	455	439	419	396	361

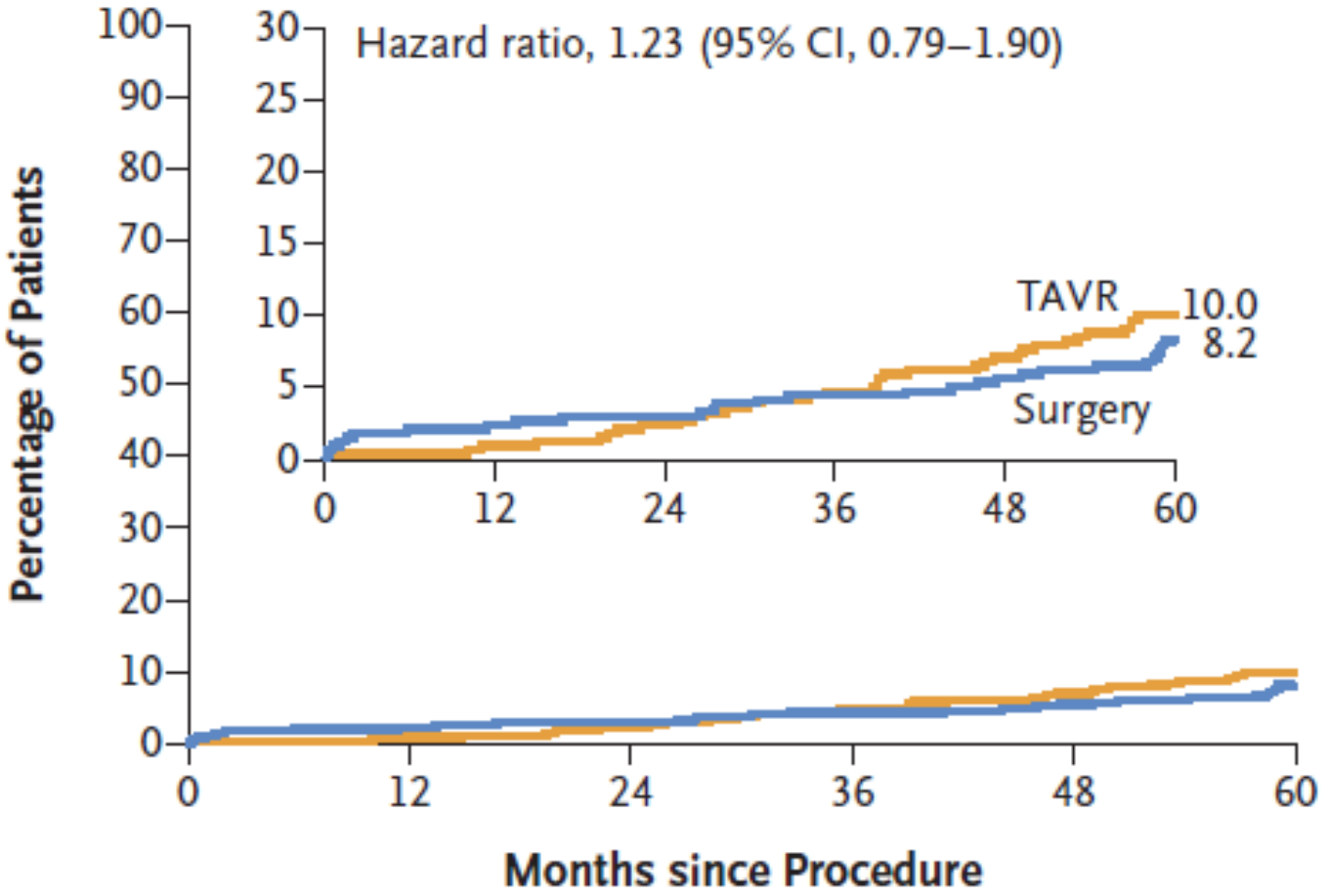
Death from Any Cause, Stroke, or Rehospitalization



No. at Risk

Surgery	454	372	349	328	309	276
TAVR	496	453	434	415	391	353

Death from Any Cause



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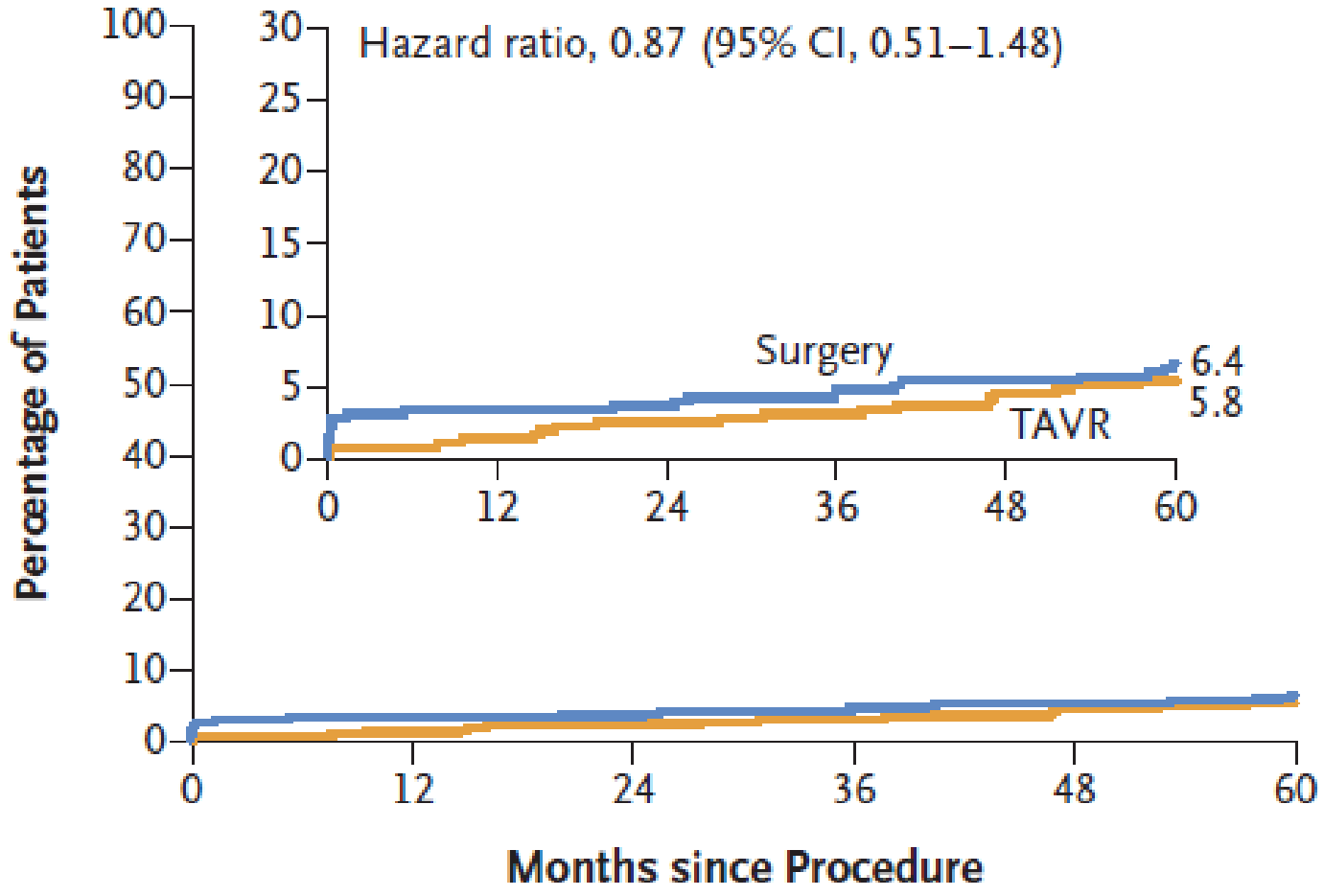
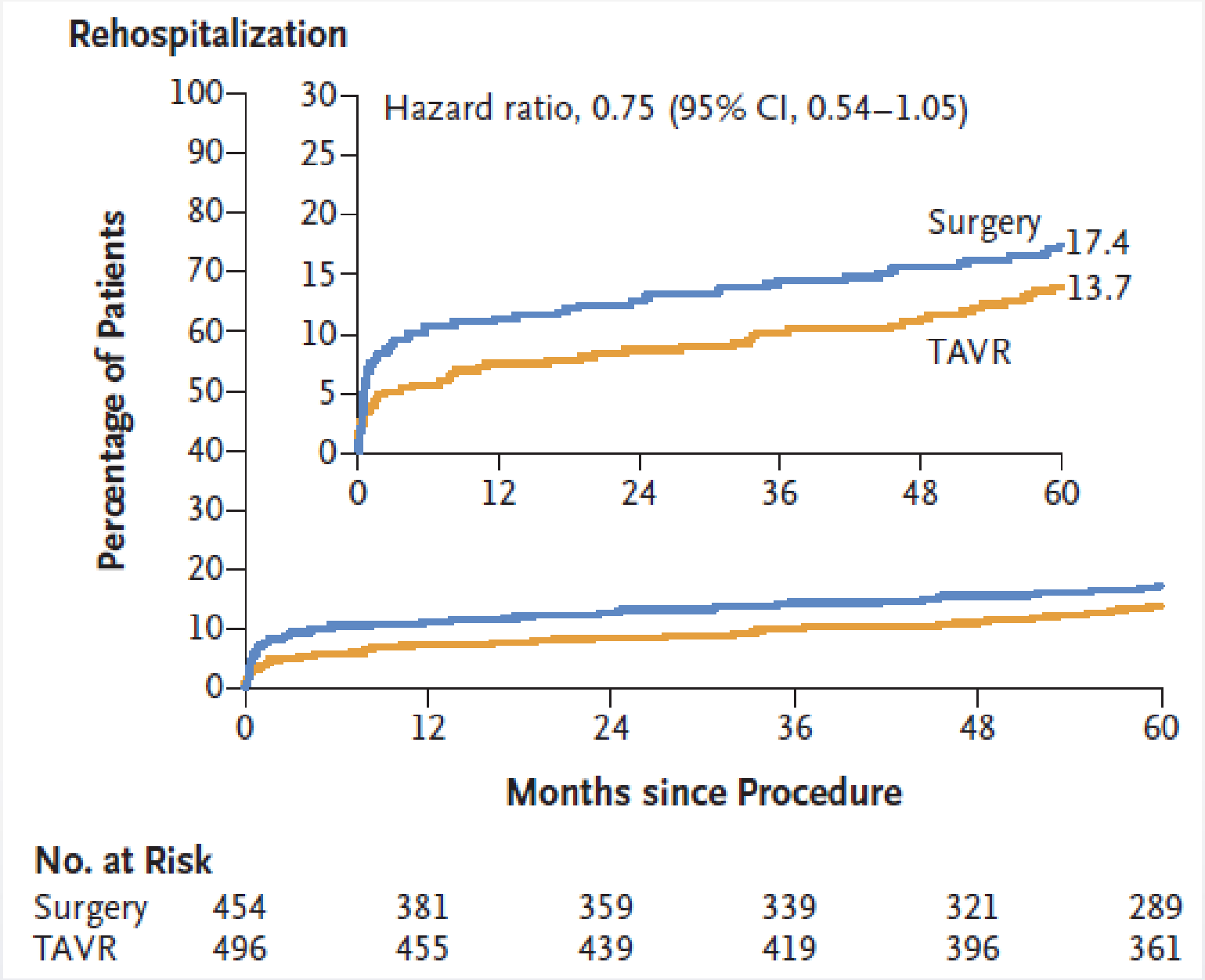
Stroke



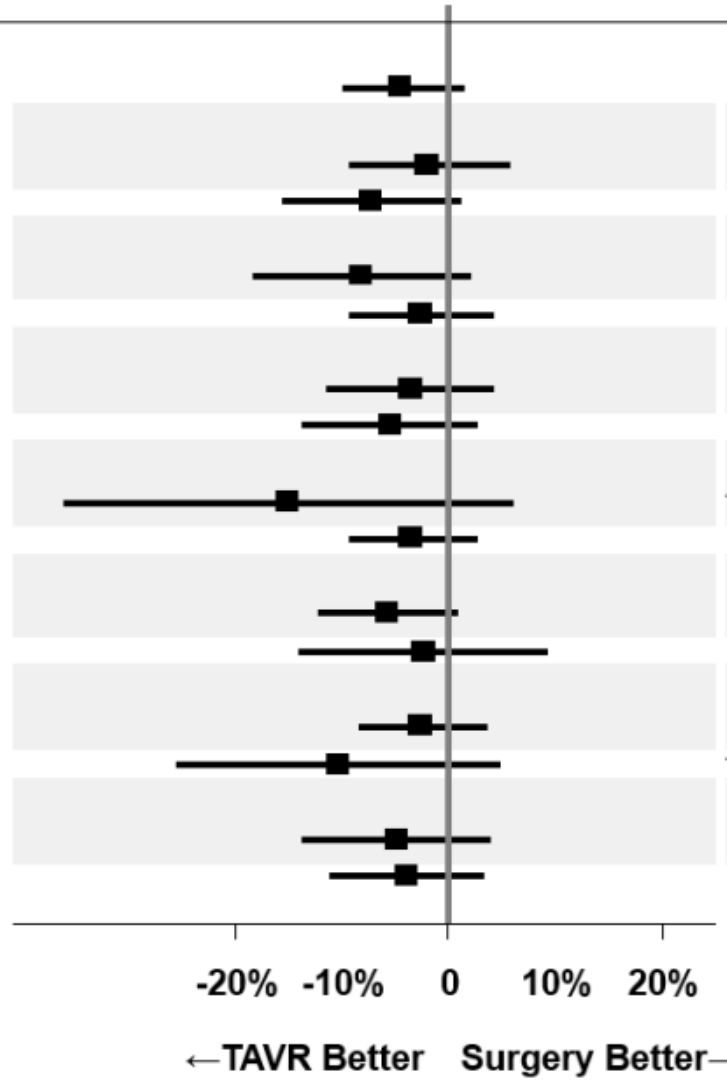
No. at Risk

Surgery	454	416	397	378	361	329
TAVR	496	486	468	450	428	391

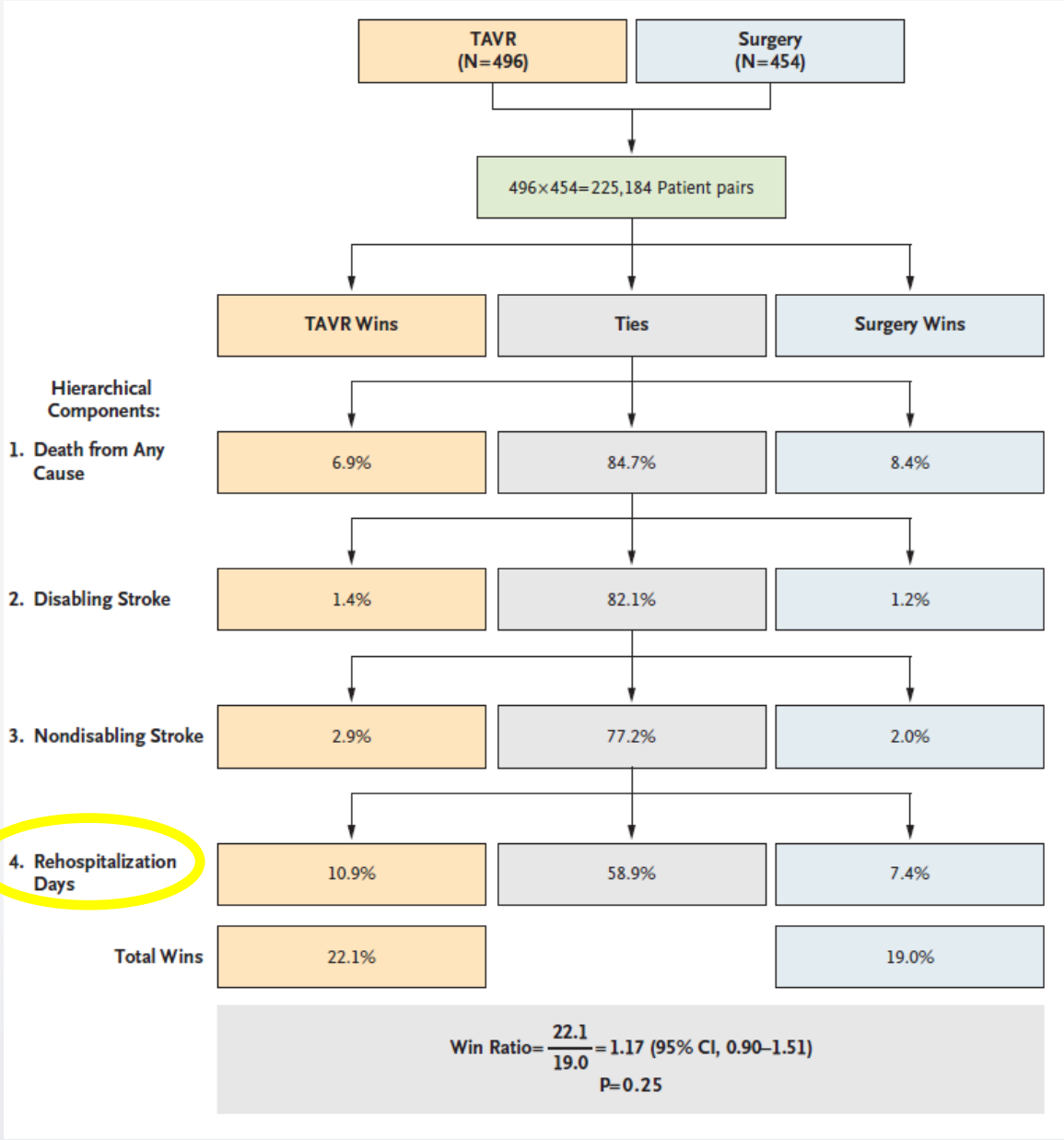

Rehospitalization
Hazard ratio, 0.75 (95% CI, 0.54–1.05)
Surgery
17.4
13.7
TAVR
Percentage of Patients
100
90
80
70
60
50
40
30
20
10
0
30
25
20
15
10
5
0
0
12
24
36
48
60
Months since Procedure
No. at Risk
Surgery 454 381 359 339 321 289
TAVR 496 455 439 419 396 361

Subgroups at 5 Years (Primary Endpoint)

Subgroup	TAVR	Surgery	Difference (TAVR – Surgery) [95% CI]
Overall	**22.8%**	**27.2%**	**-4.3% [-10.0%, 1.3%]**
Age, y			
≤ 74 (n=516)	23.9%	25.8%	-1.9% [-9.5%, 5.7%]
> 74 (n=434)	21.6%	28.8%	-7.2% [-15.6%, 1.2%]
Sex			
Female (n=292)	21.4%	29.5%	-8.1% [-18.4%, 2.2%]
Male (n=658)	23.6%	26.2%	-2.6% [-9.4%, 4.1%]
STS Score, %			
≤ 1.8 (n=464)	21.6%	25.1%	-3.5% [-11.4%, 4.3%]
> 1.8 (n=486)	23.9%	29.4%	-5.5% [-13.6%, 2.7%]
LVEF, %			
≤ 55 (n=89)	26.6%	41.5%	-15.0% [-36.0%, 6.1%]
> 55 (n=819)	22.0%	25.4%	-3.4% [-9.3%, 2.6%]
NYHA Class			
I/II (n=687)	20.4%	26.1%	-5.7% [-12.2%, 0.7%]
III/IV (n=263)	28.3%	30.6%	-2.3% [-13.9%, 9.3%]
Atrial Fibrillation			
No (n=786)	21.2%	23.7%	-2.5% [-8.5%, 3.5%]
Yes (n=163)	31.9%	42.4%	-10.4% [-25.6%, 4.8%]
KCCQ-OS Score			
≤ 70 (n=407)	24.6%	29.4%	-4.9% [-13.7%, 4.0%]
> 70 (n=536)	21.3%	25.2%	-3.9% [-11.2%, 3.4%]



Breakdown of Win Ratio Analysis



Other Outcomes Through 5 Years

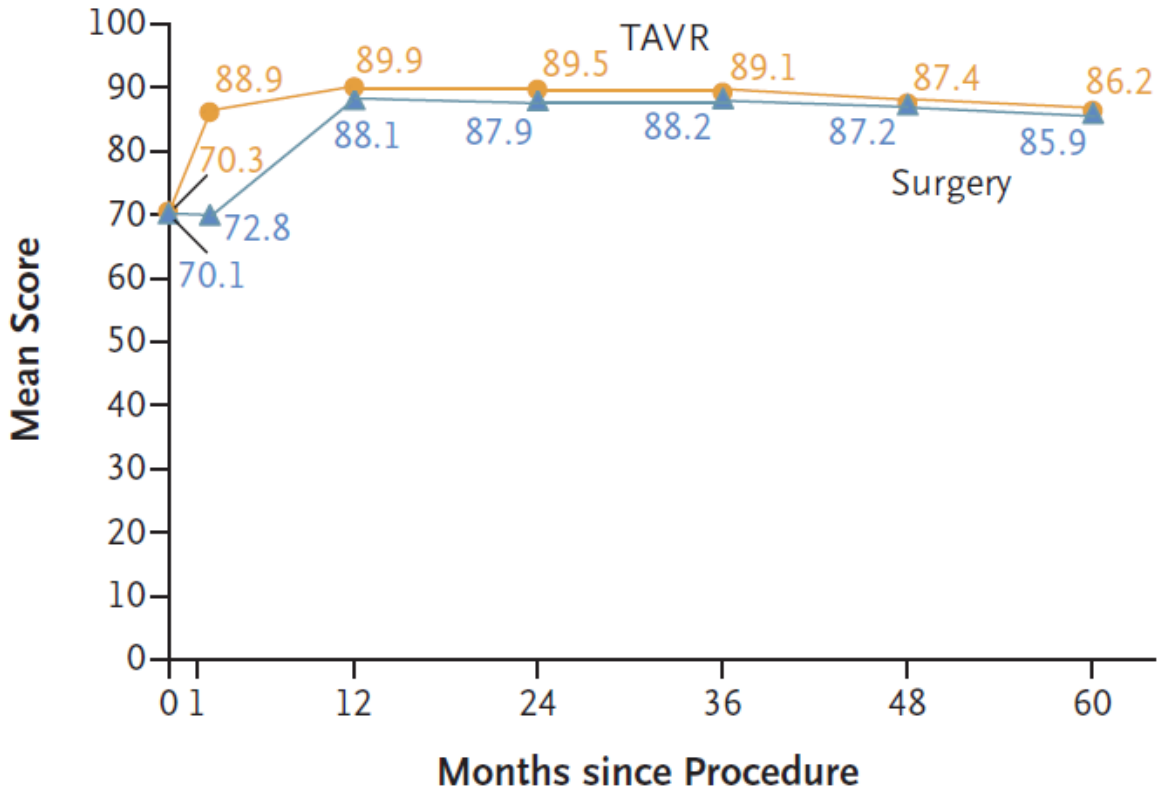
End Point	Baseline to 5 Years			1 Year to 5 Years		
	TAVR (N=496)	Surgery (N=454)	Hazard Ratio (95% CI)	TAVR (N=490)	Surgery (N=427)	Hazard Ratio (95% CI)
	no. of patients with event (Kaplan–Meier estimate, %)			*no. of patients with event (Kaplan–Meier estimate, %)*		
Aortic-valve reintervention	12 (2.6)	12 (3.0)	0.86 (0.39–1.92)	9 (2.0)	10 (2.6)	0.77 (0.31–1.90)
Endocarditis	6 (1.3)	8 (2.0)	0.65 (0.23–1.87)	5 (1.1)	6 (1.5)	0.72 (0.22–2.35)
Valve thrombosis¶	12 (2.5)	1 (0.2)	10.52 (1.37–80.93)	10 (2.1)	1 (0.2)	8.72 (1.12–68.12)
New-onset atrial fibrillation‖**	55 (13.7)	155 (42.4)	0.25 (0.19–0.34)	21 (6.0)	5 (2.6)	2.30 (0.87–6.10)
New pacemaker‖**	63 (13.5)	43 (10.4)	1.33 (0.90–1.96)	25 (6.1)	18 (4.9)	1.22 (0.67–2.24)
Serious bleeding‖	49 (10.2)	64 (14.8)	0.65 (0.45–0.95)	25 (5.6)	18 (5.1)	1.15 (0.63–2.11)

- A lot more early A-fib with SAVR
- A little more early bleeding with SAVR
- A little more early pacemaker need with TAVR

- No clear trend in complications from years 1-5

Quality of Life

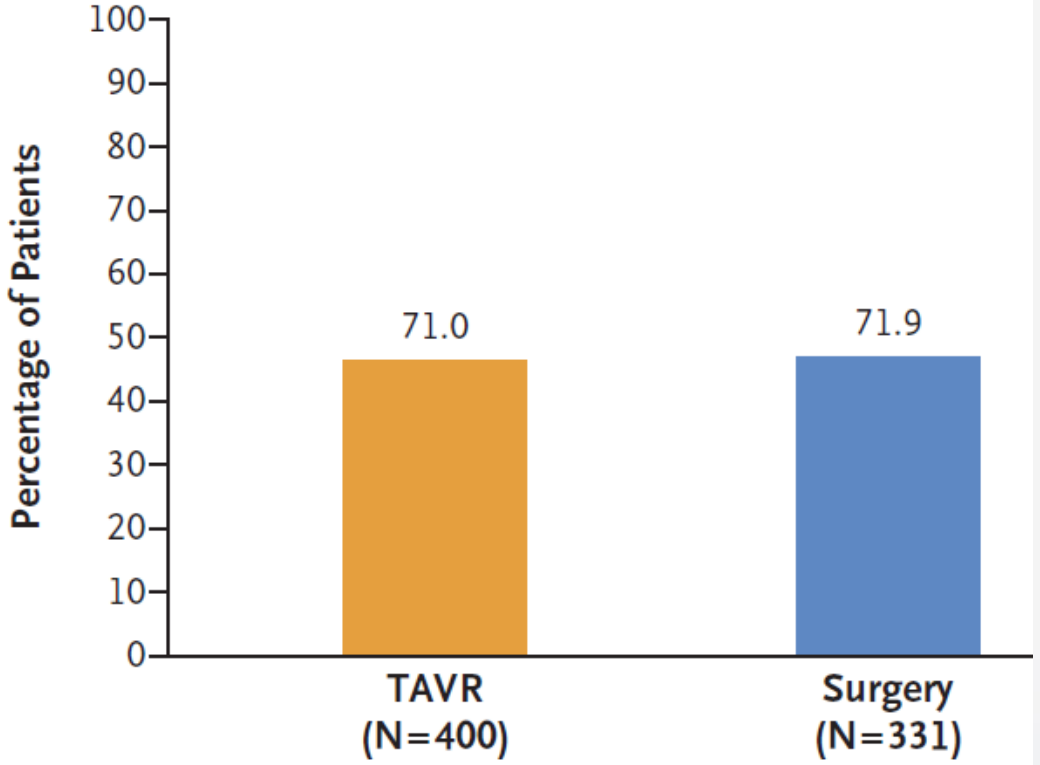
KCCQ-OS Scores



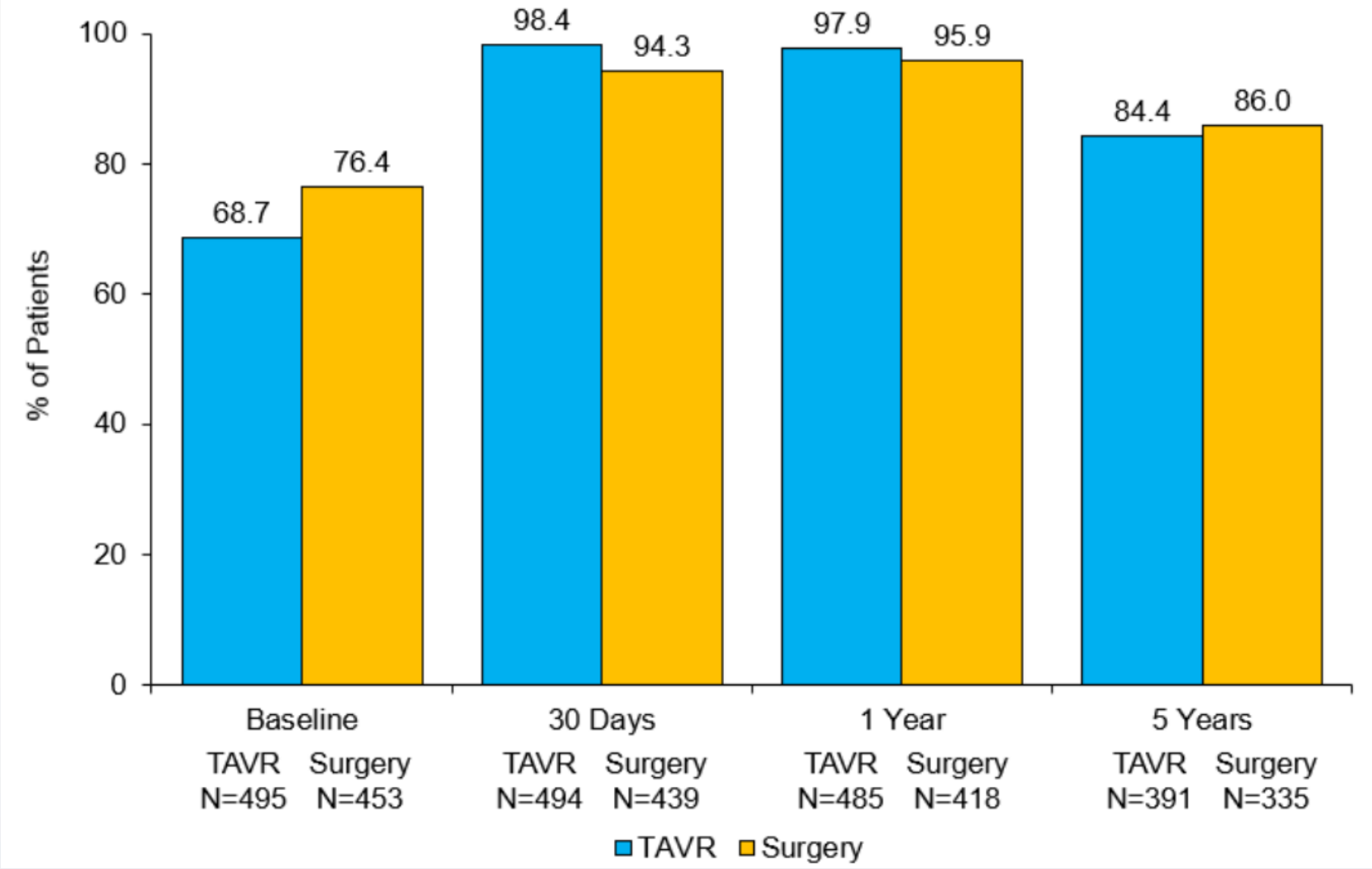
No. at Risk

TAVR	493 491	481	444	406	381	354
Surgery	448 433	403	367	340	321	301

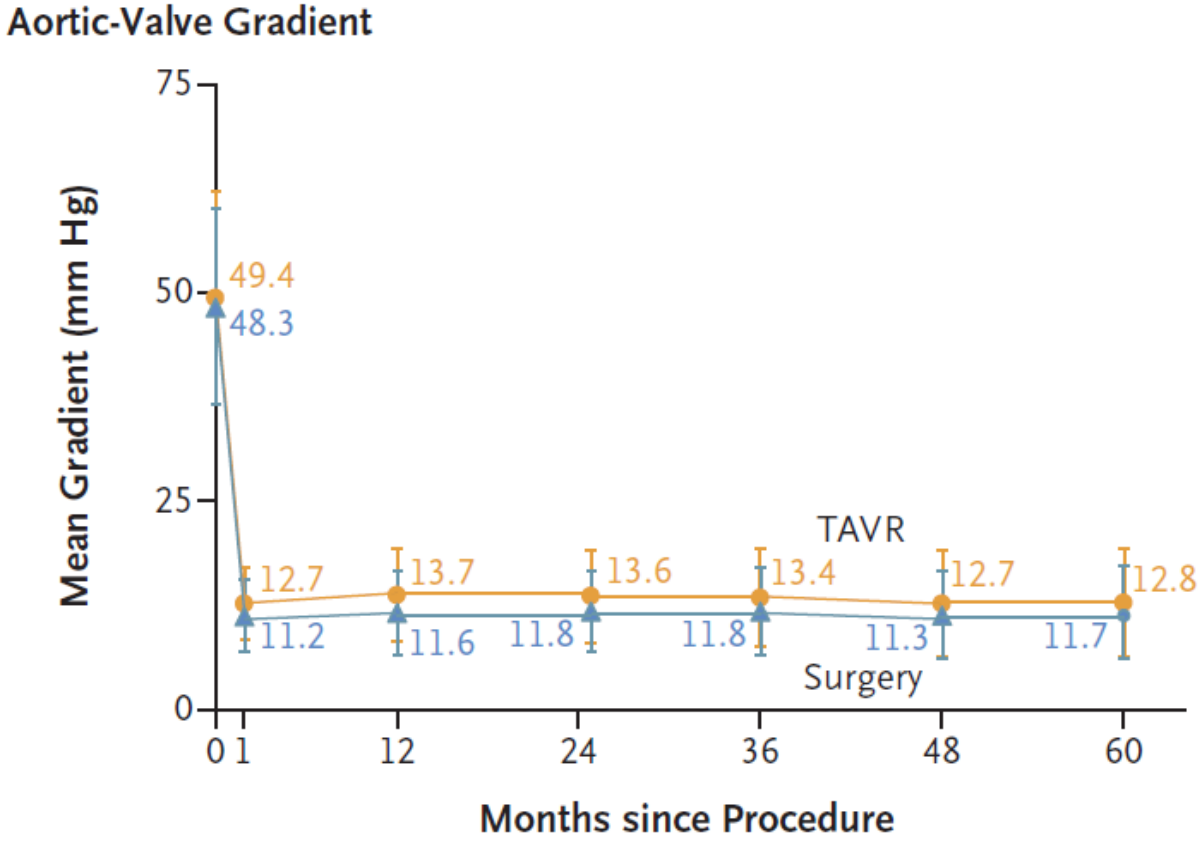
Patients Who Were Alive with KCCQ-OS Score ≥75

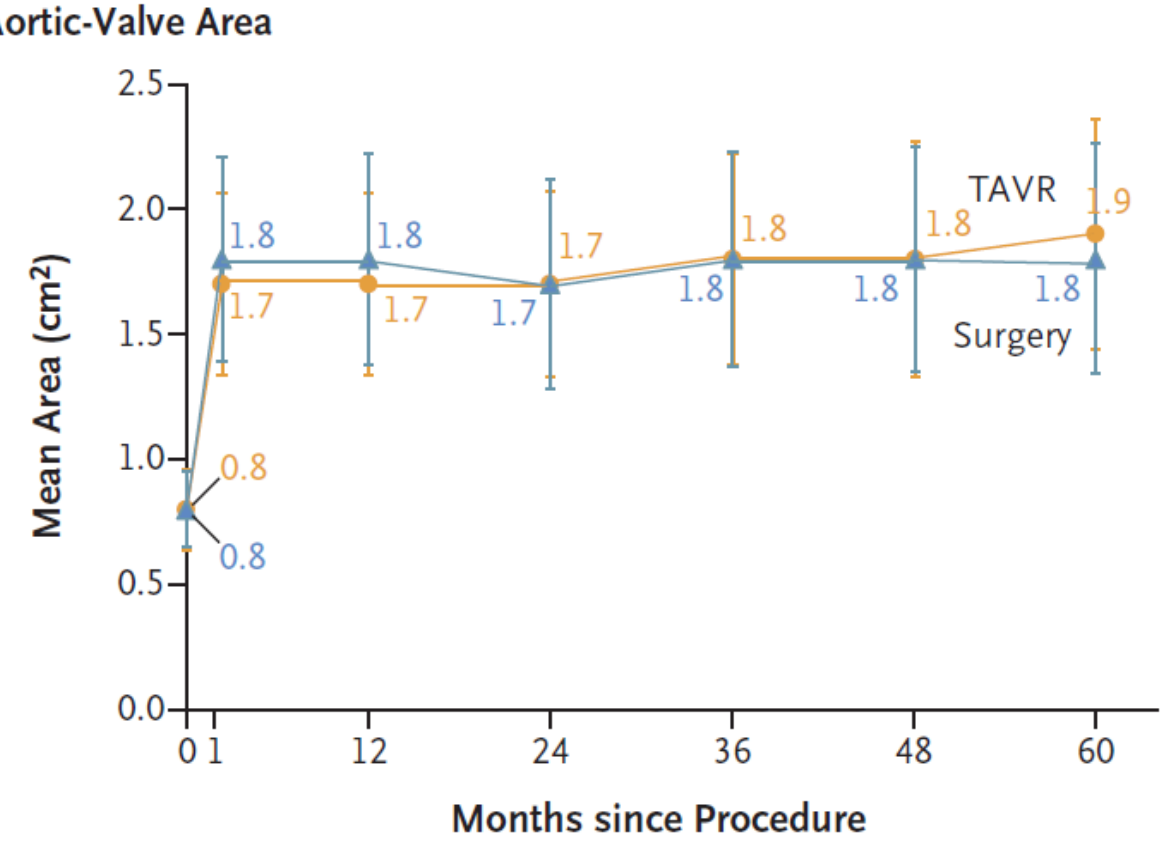


NYHA Class I or II



Durability - Hemodynamics





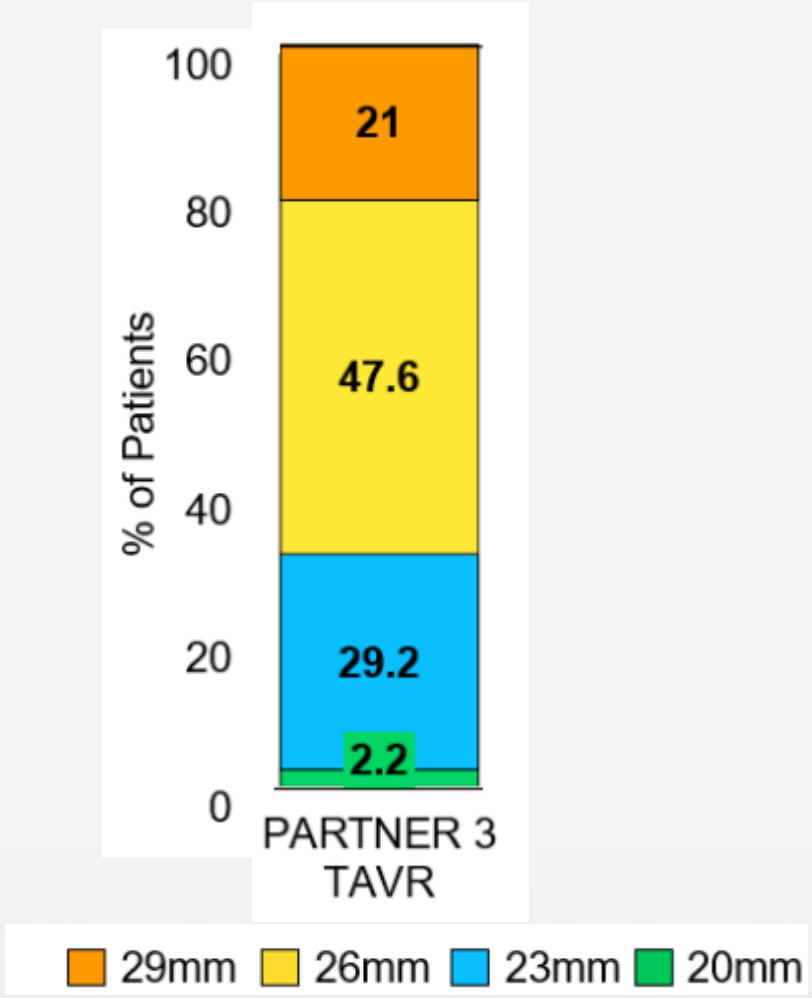
No. at Risk

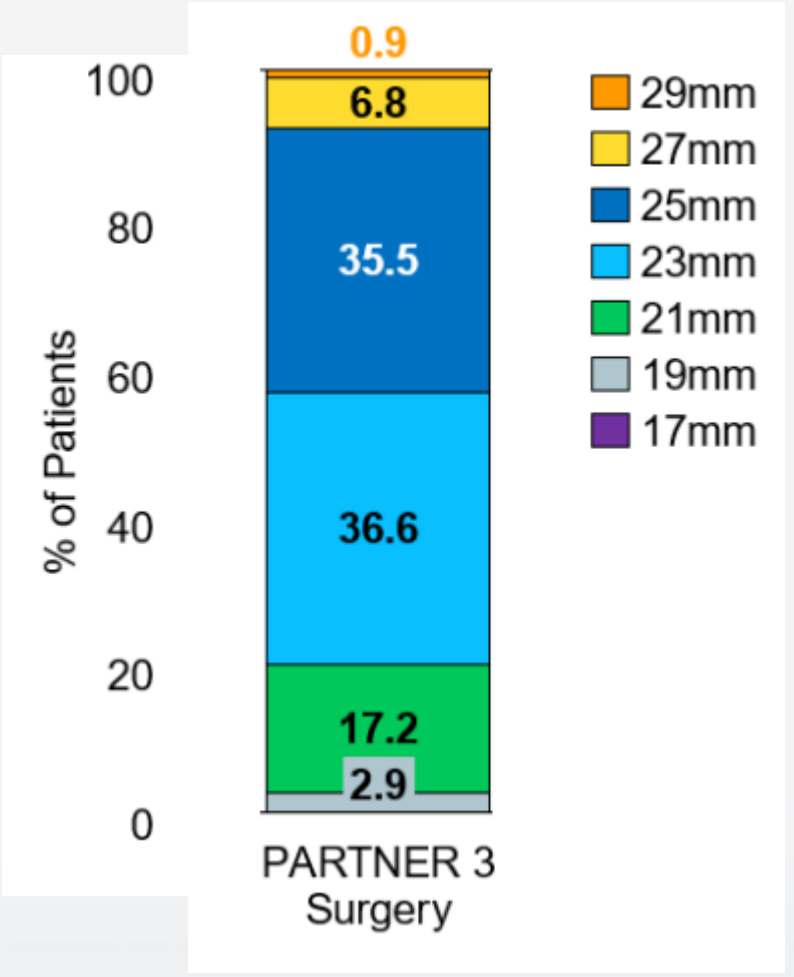
TAVR	483	492	474	437	372	348	329
Surgery	442	432	391	360	304	305	282

No. at Risk

TAVR	458	482	450	416	347	334	320
Surgery	424	415	371	342	289	295	275

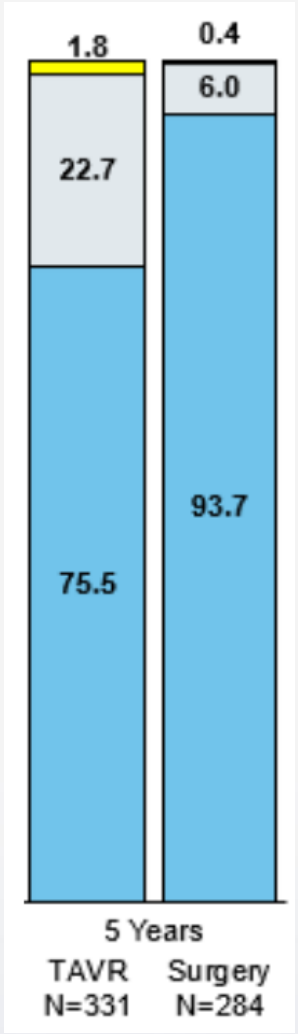
Valve Sizes


100
80
60
40
20
0
% of Patients
21
47.6
29.2
2.2
PARTNER 3
TAVR
29mm
26mm
23mm
20mm

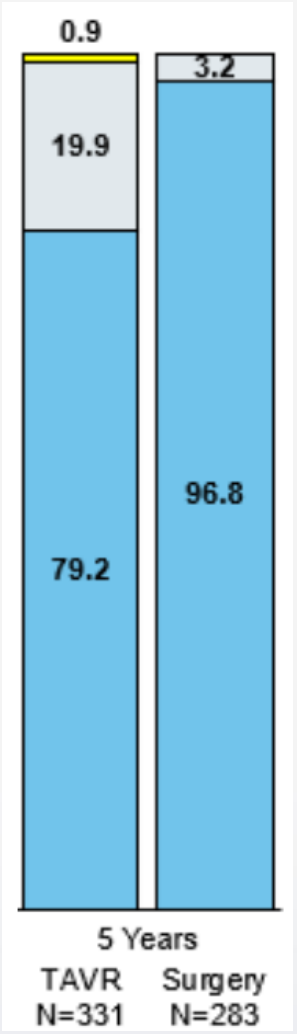

100
80
60
40
20
0
% of Patients
0.9
6.8
35.5
36.6
17.2
2.9
PARTNER 3
Surgery
29mm
27mm
25mm
23mm
21mm
19mm
17mm

Aortic Regurgitation

Total



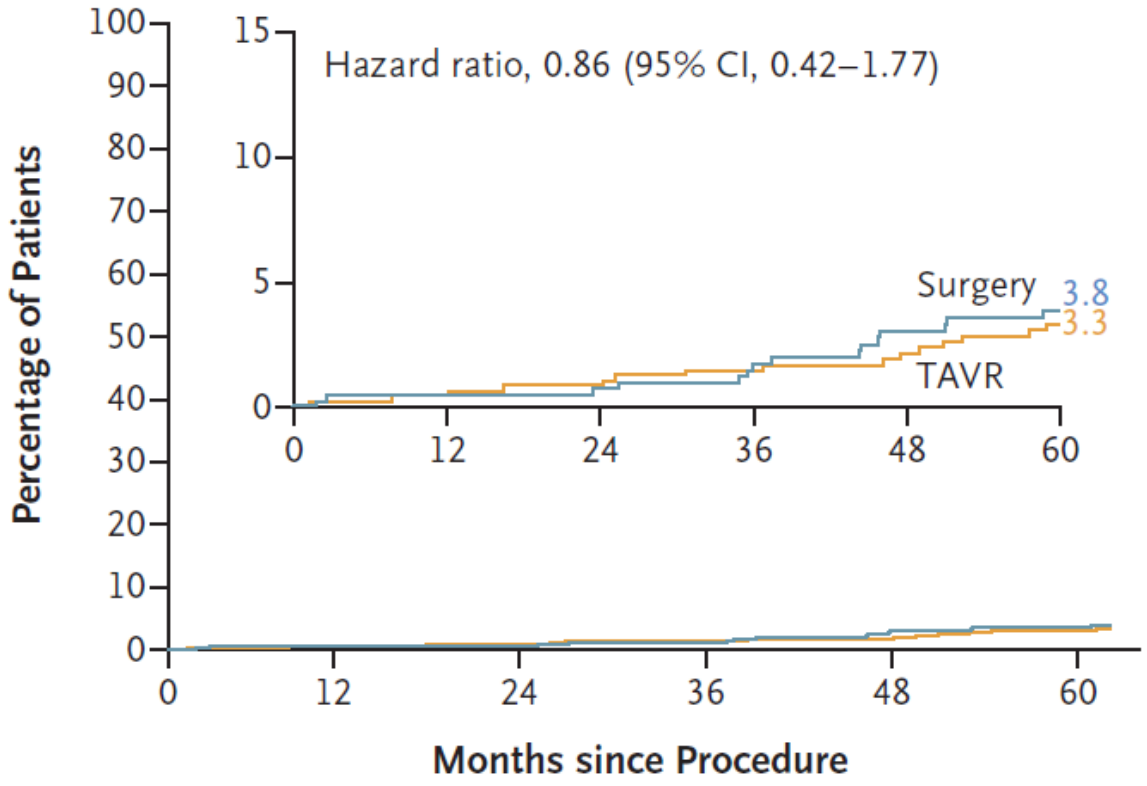
Paravalvular



None/Trace Mild Moderate

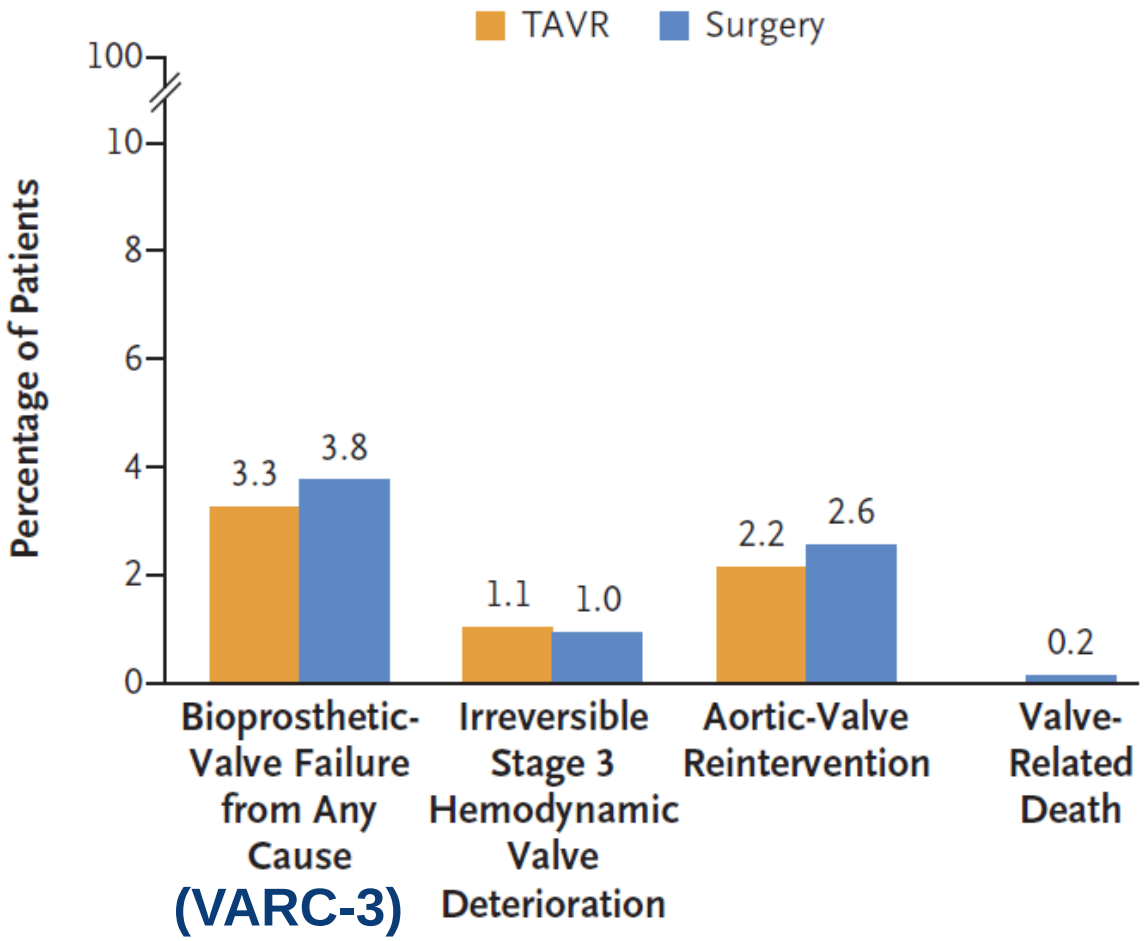
Durability - Clinical

Bioprosthetic-Valve Failure



No. at Risk						
TAVR	496	489	475	454	430	392
Surgery	454	426	407	390	369	334

Bioprosthetic-Valve Failure and Components at 5 Yr



Key Takeaways

- In low risk patients, TAVR with SAPIEN 3 compared to SAVR was similar at 5 years with respect to:
  - Survival
  - Complications, including stroke and rehospitalization
  - Quality of Life
  - Durability – as defined by hemodynamics and rates of valve failure

- ≥90% of TAVR and SAVR patients were alive at 5 years in the PARTNER 3 Trial

- At 5 years, valve failure (<4.0%) and reintervention (≤3.0%) are very low for both TAVR with SAPIEN 3 and SAVR

- In my opinion, there is no plausible reason to suspect that a SAPIEN 3 valve will be less durable than a bioprosthetic surgical valve beyond 5 years (10 year f/u planned)

Lifetime Management - Some Will Outlive the 1st Valve

- A small but significant number of low-risk patients should be expected to outlive their first prosthetic valve, whether it be TAVR or SAVR

- The second procedure is most likely to be a TAVR
  - Valve-in-Valve TAVR of a surgical valve
  - TAV-in-TAV

- Care and attention to a potential 2nd valve should be undertaken before the 1st
  - For SAVR – no supra-annular valves, largest valve possible, consider aortic root enlargement, consider valve suitable for further expansion
  - For TAVR – pay attention to coronary heights and Sinus widths, place TAVR valve at height and with a commissural alignment that will best accommodate a second valve

Surgical Explantation After TAVR Failure

Mid-Term Outcomes From the EXPLANT-TAVR International Registry

269 patients

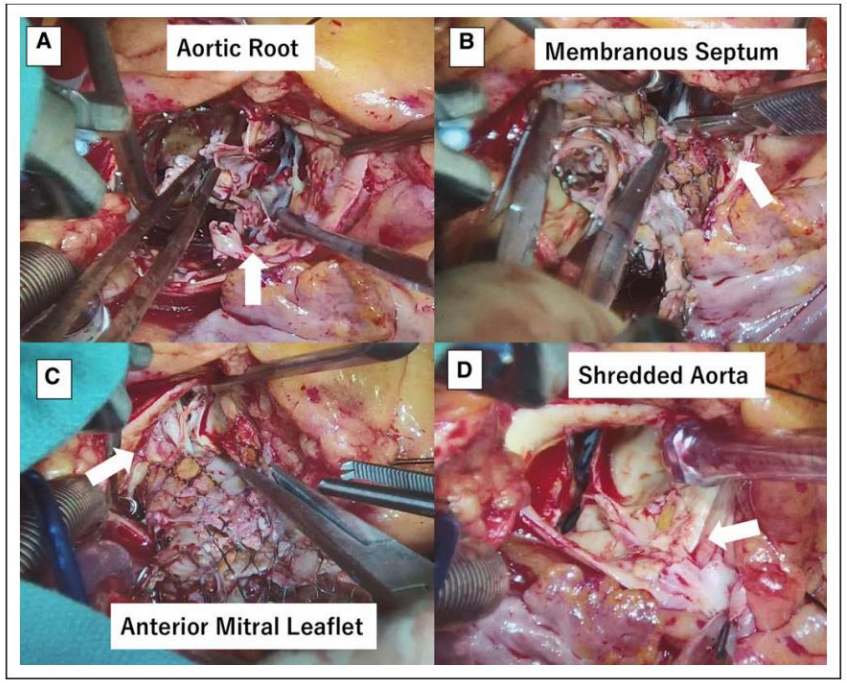
Mean age 72.7 ± 10.4 years

Mean time to failure 11.5 mo

STS score 3.2% at TAVR

STS score 5.0% at explant

11.9% in-hospital mortality



Short- and Mid-Term Outcomes After Transcatheter Aortic Valve Replacement Explantation (N = 269)

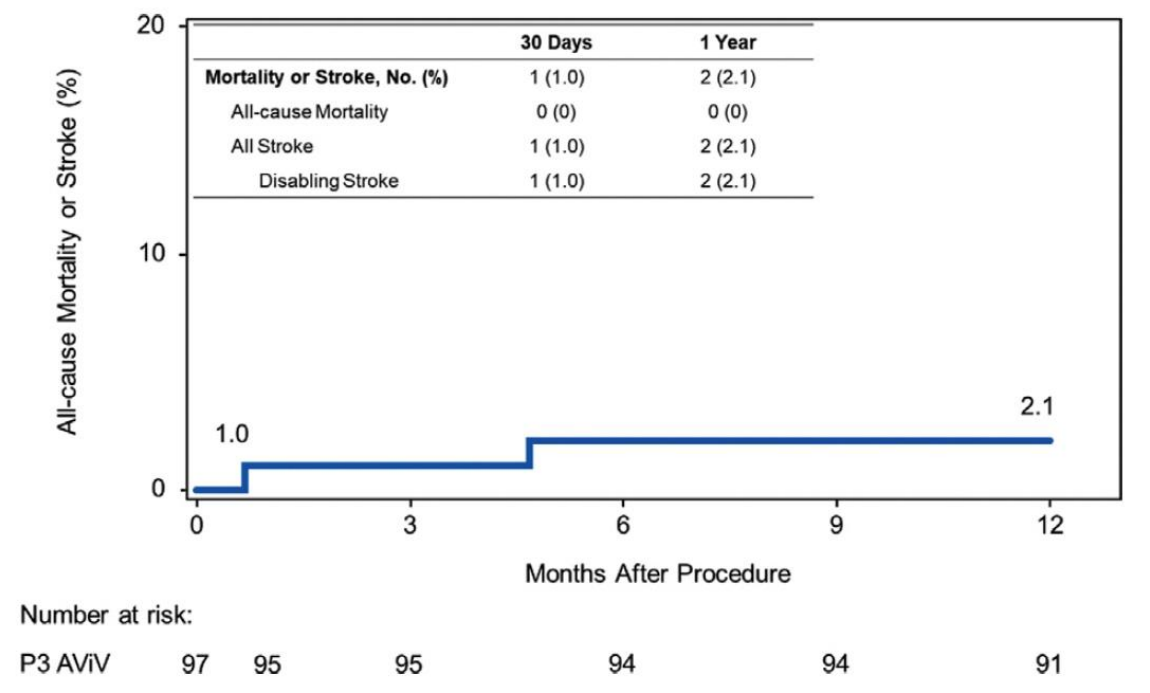
Follow-up (mo) post explantation	14.6 ± 20.7
30 d	
Mortality	34 (13.1)
Stroke	18 (8.6)
Readmission	28 (13.7)
Follow-up complete	259 (97.7)
1 y	
Mortality	53 (28.5)
Stroke	23 (18.7)
Follow-up complete	186 (86.1)

Bapat VN, et al. *JACC Int* 2021;14:1978-1991.

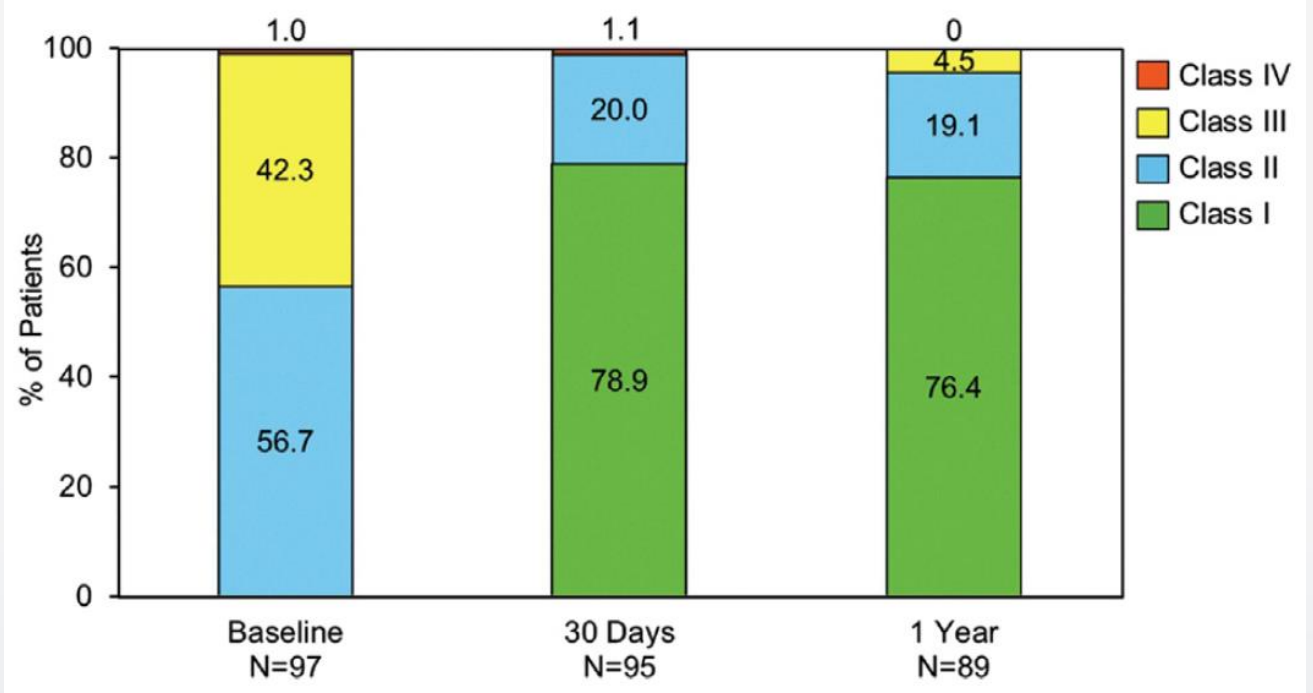
Brescia BA, et al. *Cirv CV Invt* 2021;14:e009927.

Structural Heart

Transcatheter Aortic Valve Implantation for Bioprosthetic Valve Failure: Placement of Aortic Transcatheter Valves 3 Aortic Valve-in-Valve Study



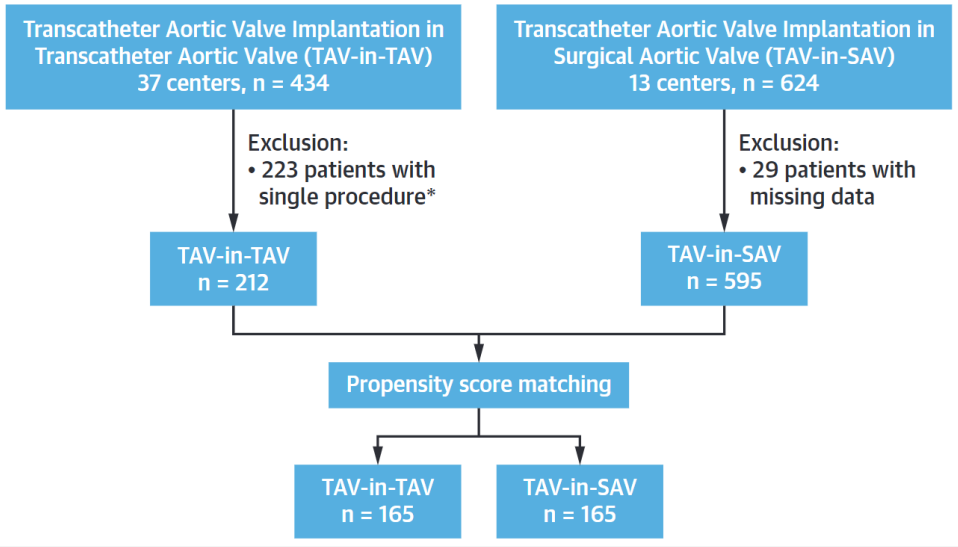
	30 Days	1 Year
Mortality or Stroke, No. (%)	1 (1.0)	2 (2.1)
All-cause Mortality	0 (0)	0 (0)
All Stroke	1 (1.0)	2 (2.1)
Disabling Stroke	1 (1.0)	2 (2.1)

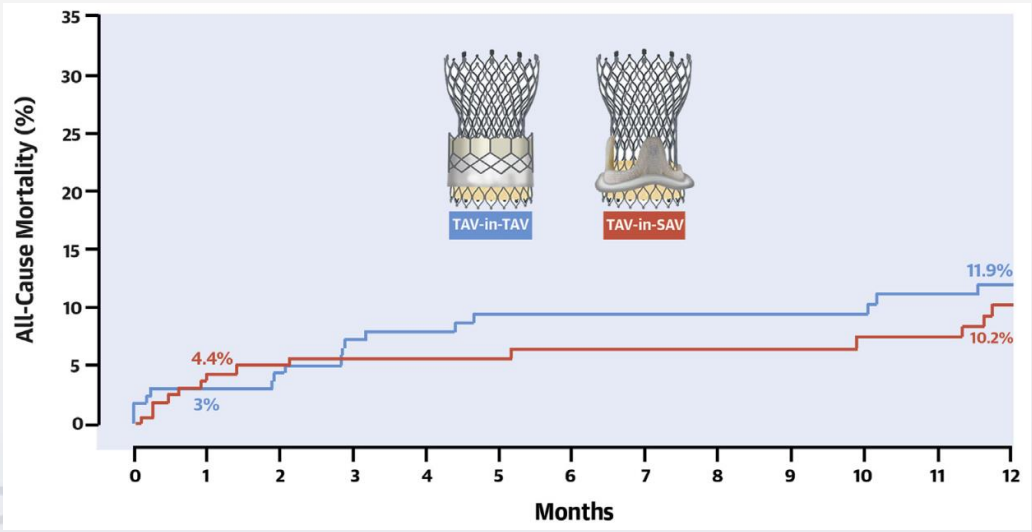


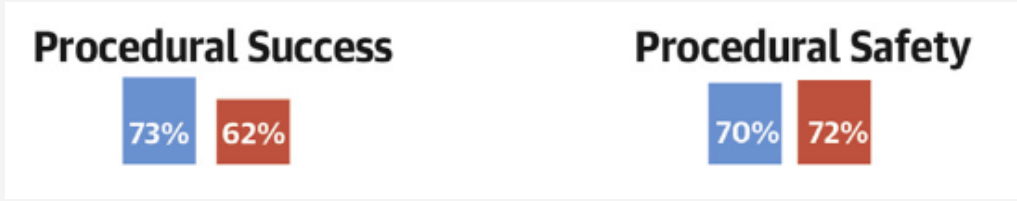
Malaisrie et al. 2022;6(6):100077

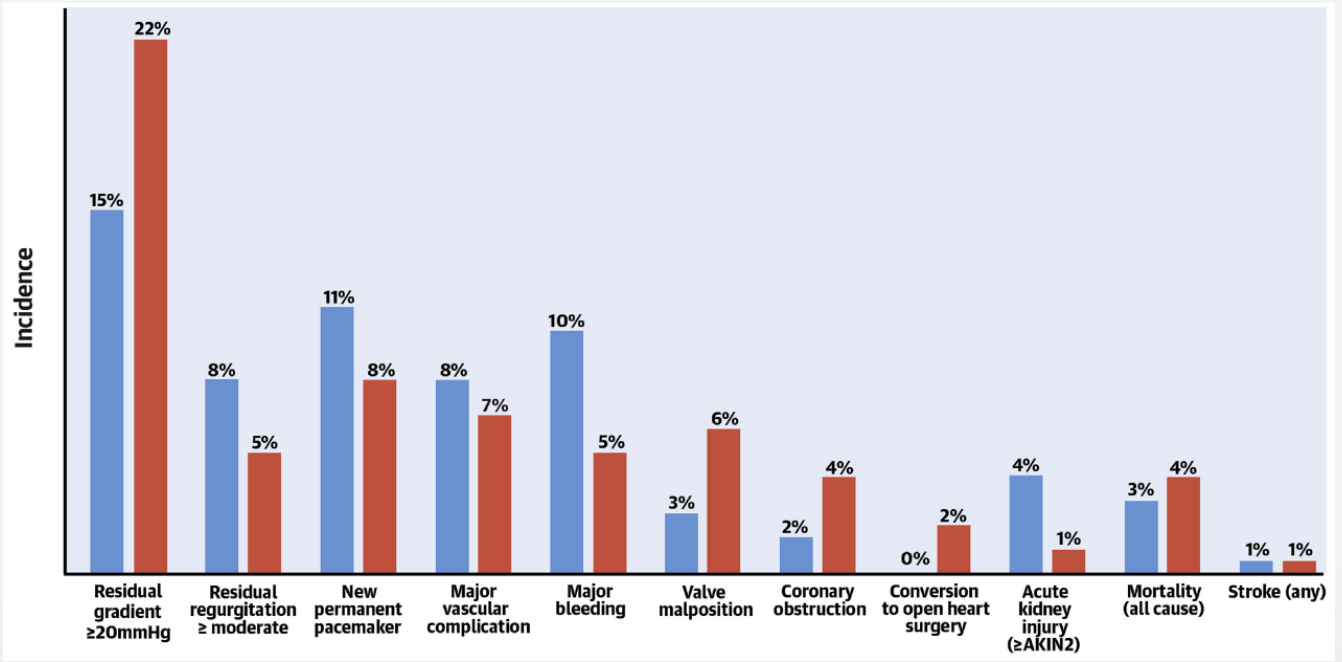
Transcatheter Replacement of Transcatheter Versus Surgically Implanted Aortic Valve Bioprostheses

Redo-TAVR international registry



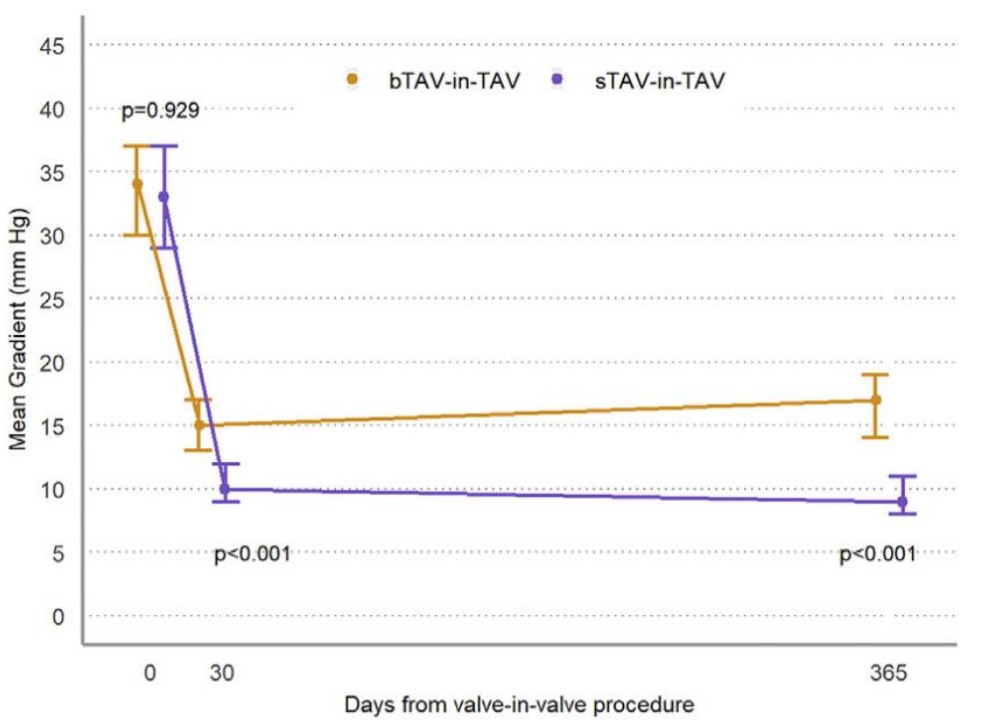


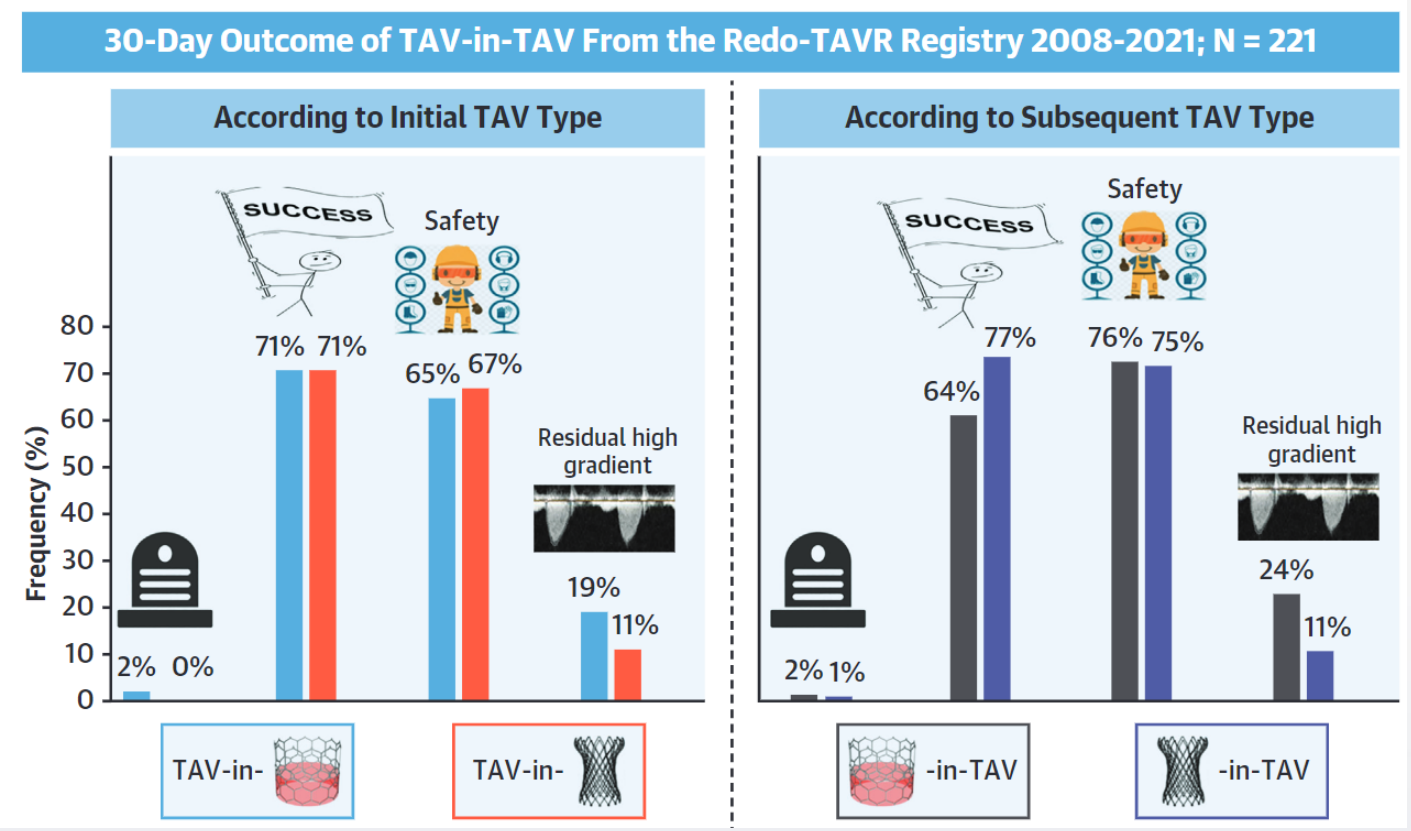




Landes U, et al. *J Am Coll Cardiol* 2021;77:1-14.

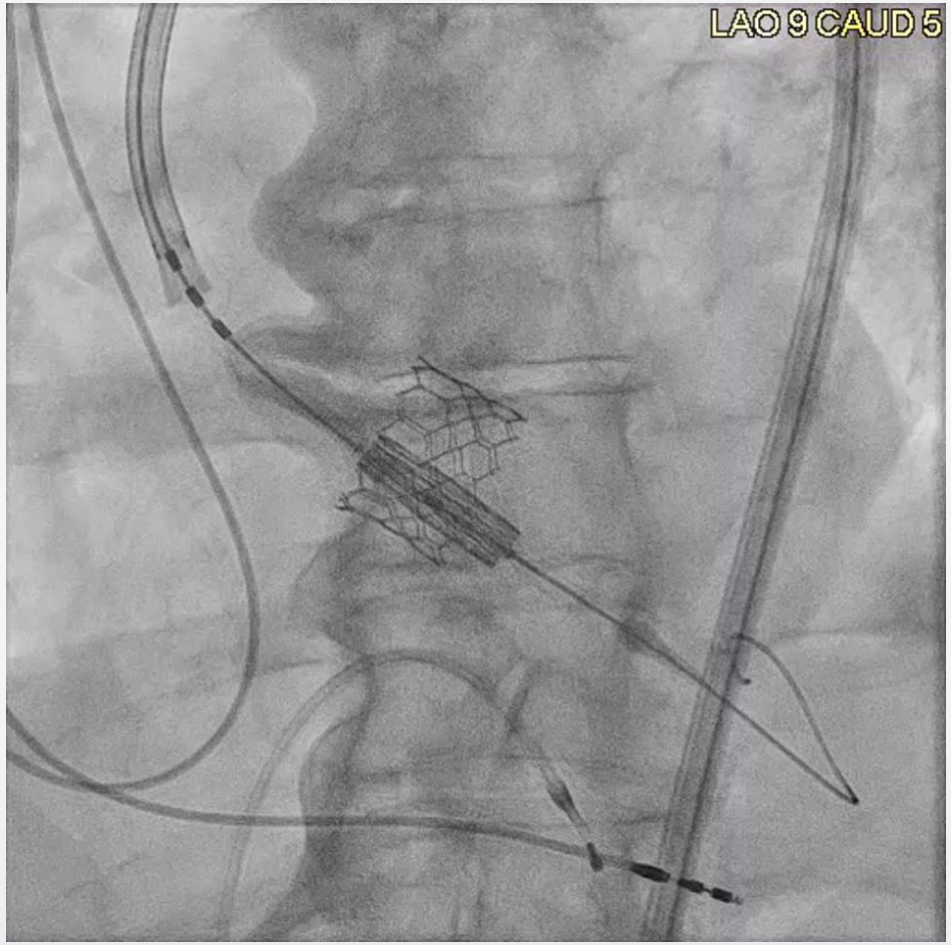
Outcomes of Redo Transcatheter Aortic Valve Replacement According to the Initial and Subsequent Valve Type

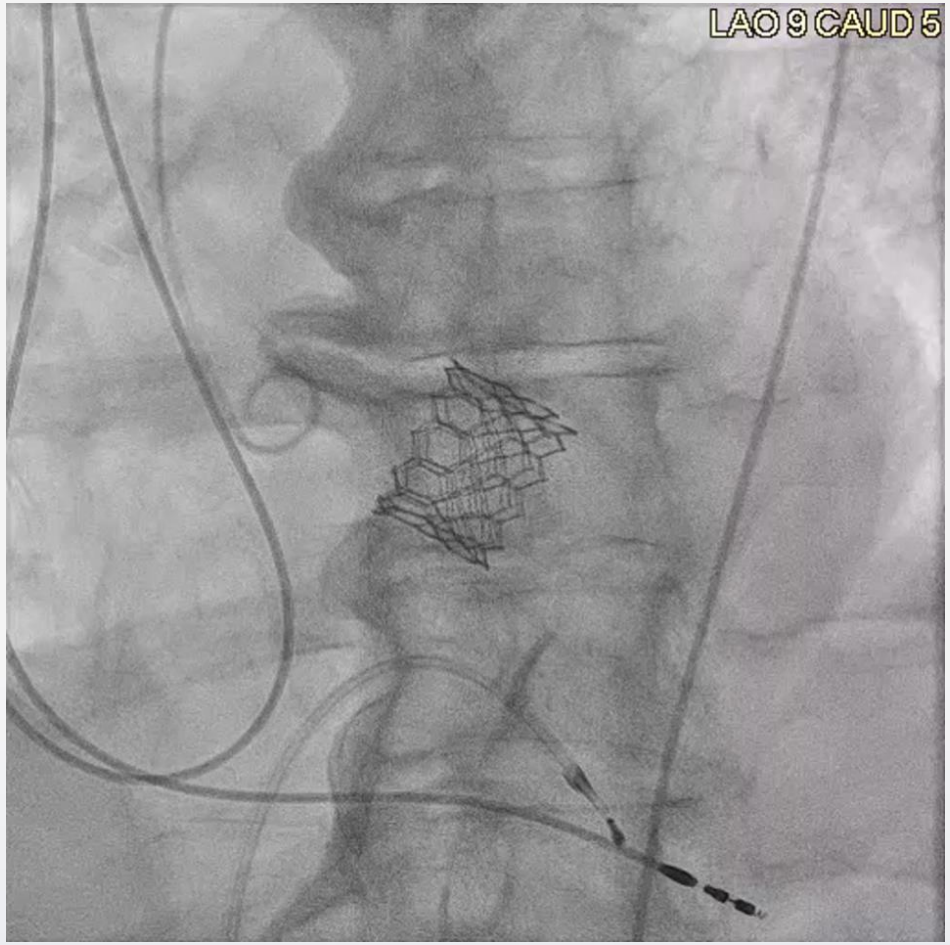




Landes U, et al. *JACC Invt* 2022;15:1543-1554.

TAV-in-TAV with a SAPIEN 3





Next day echo

- Mean gradient 14 mmHg
- Trivial paravalvular AI

Final Thoughts on Lifetime Management

- TAVR and SAVR are both reasonable 1st choices in low-risk patients
  - Current TAVR valves, including SAPIEN 3, are at least as durable as surgical valves long-term
  - Before the 1st procedure, TAVR or SAVR, anatomical considerations should be made in anticipation of a possible second procedure down the road
  - In reality, most patients will chose TAVR 1st
- To date, SAVR after TAVR has been associated with poor outcomes
- Valve-in-valve TAVR (of a surgical valve) is a very safe and effective procedure
- TAV-in-TAV, in particular SAPIEN-in-SAPIEN, is a quick and effective procedure – as long as the proper anatomical considerations were followed for the 1st TAVR