How Can We Treat Patients with Concomitant Coronary Artery Disease?

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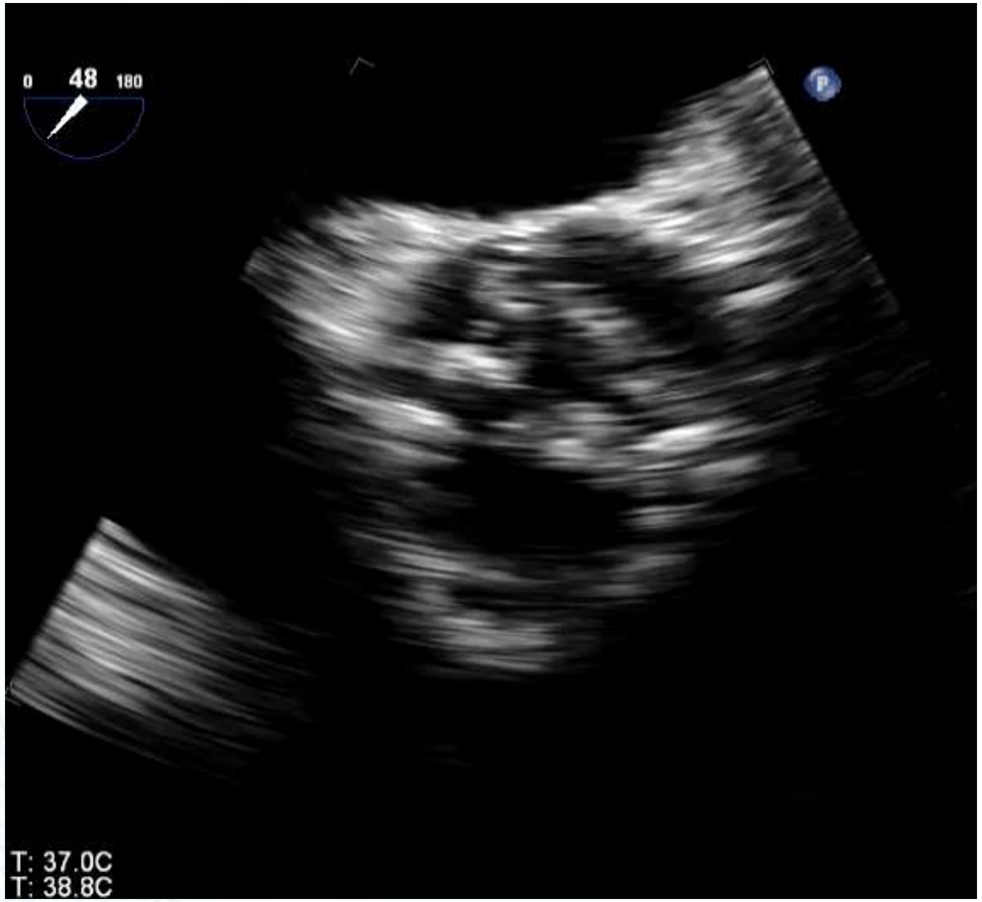
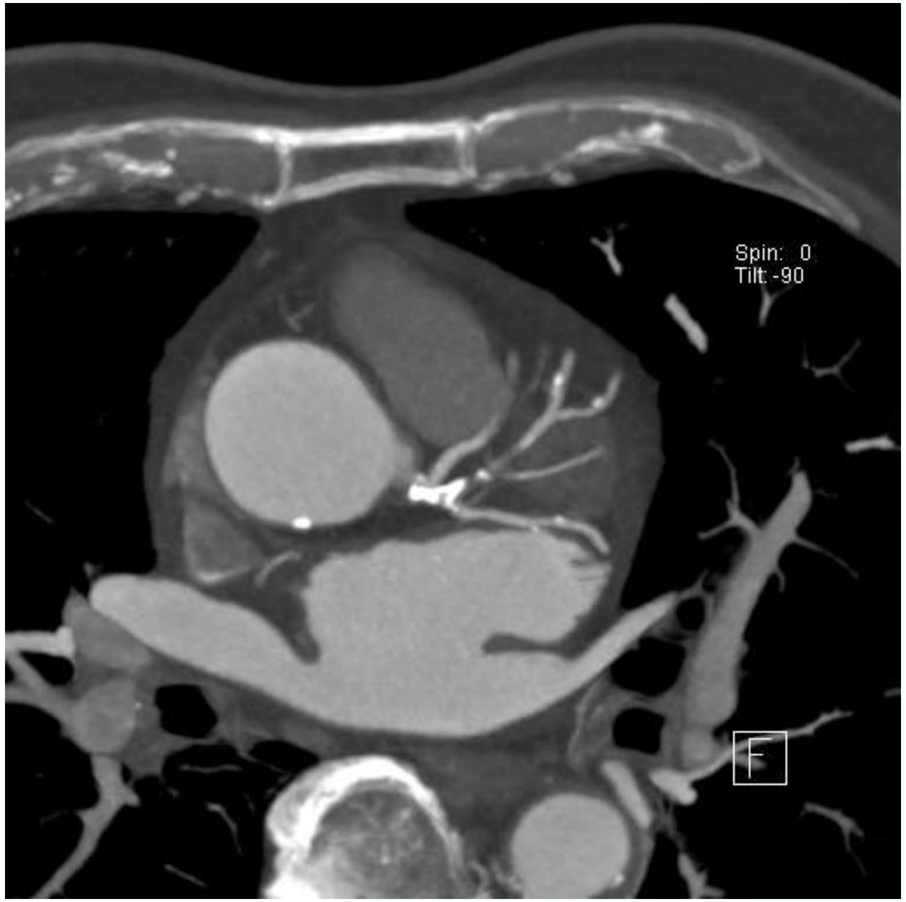
M/91 with Chest Pain

Severe AS and Severe CAD





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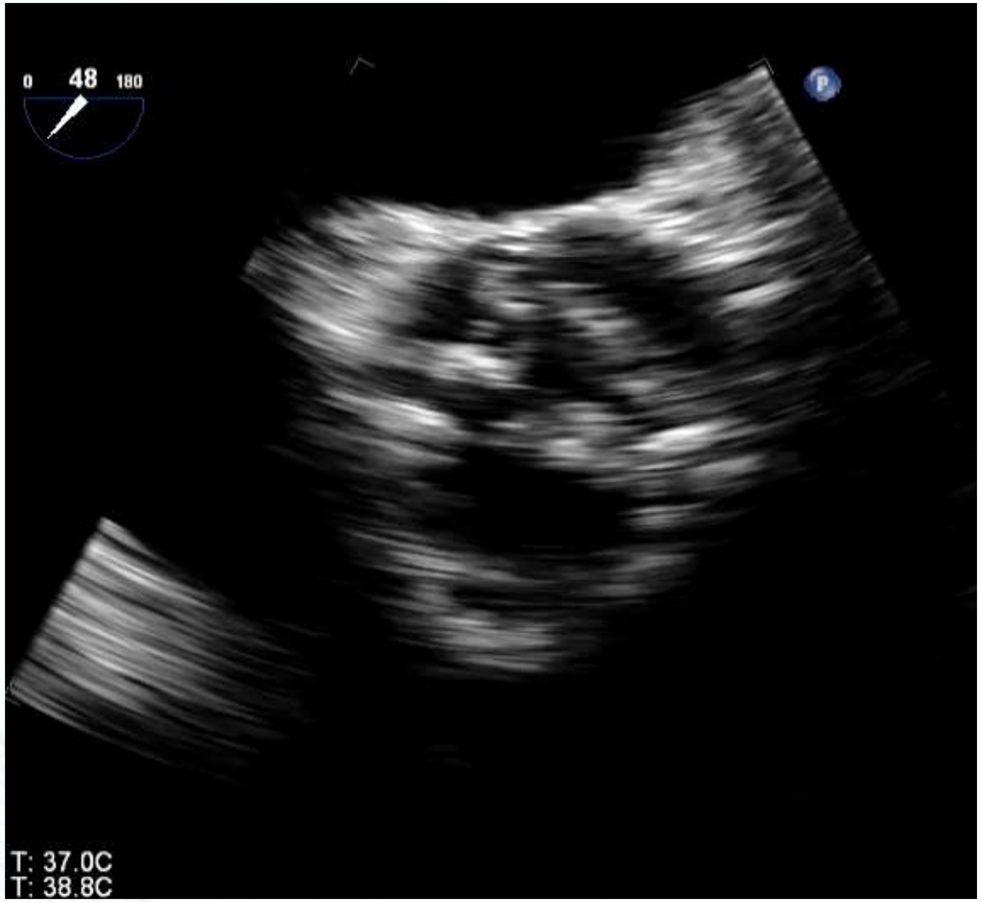
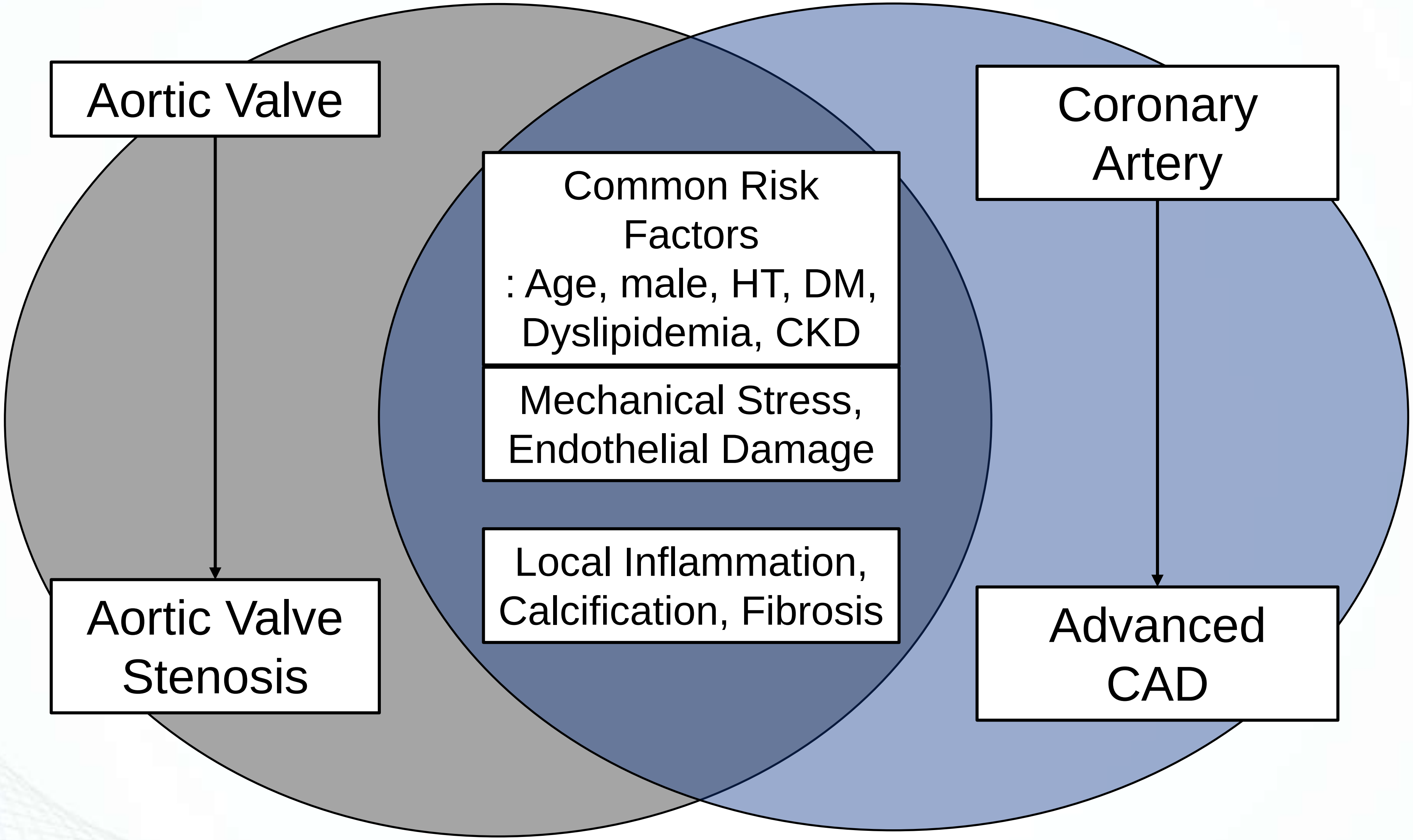
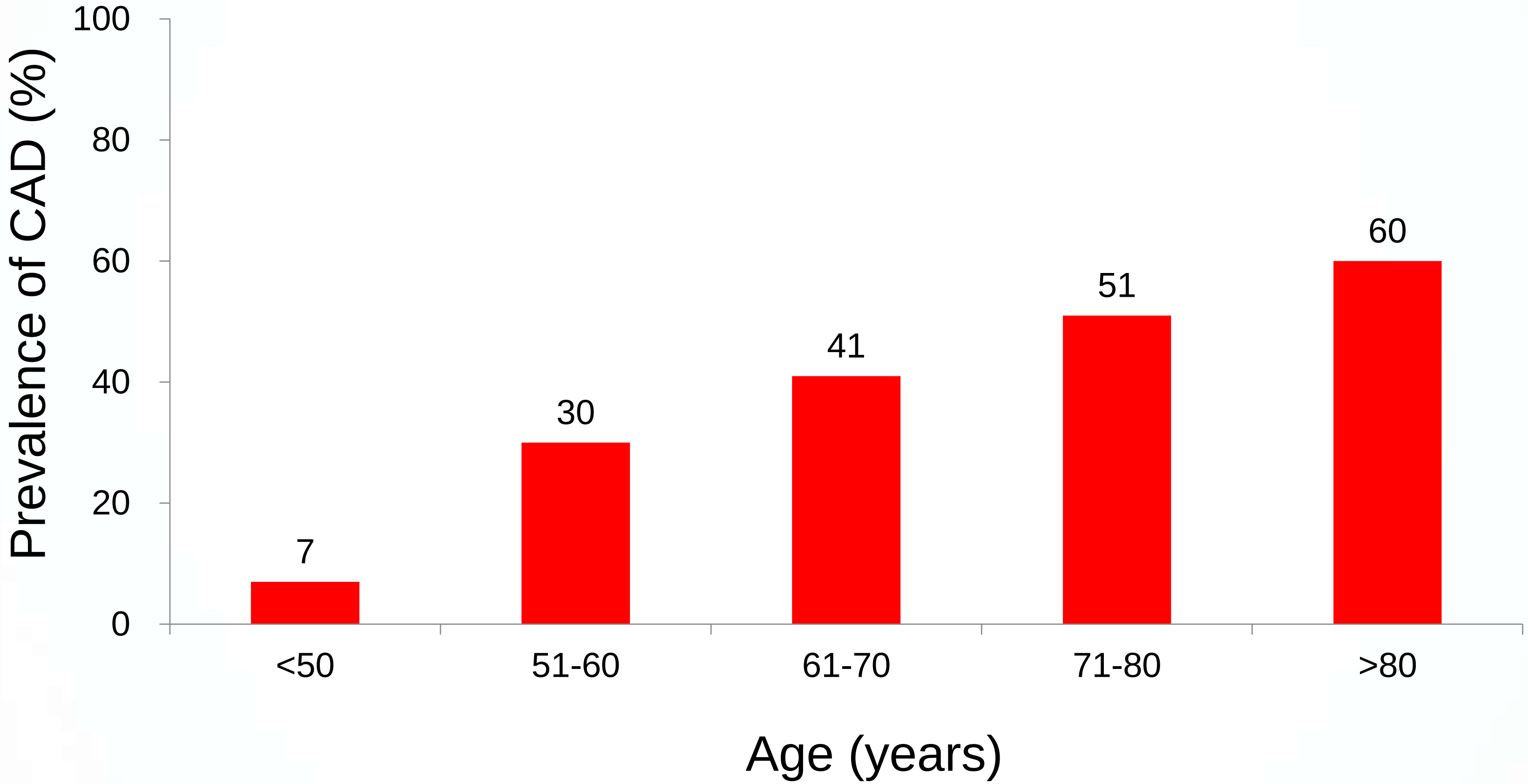


Common Pathophysiology



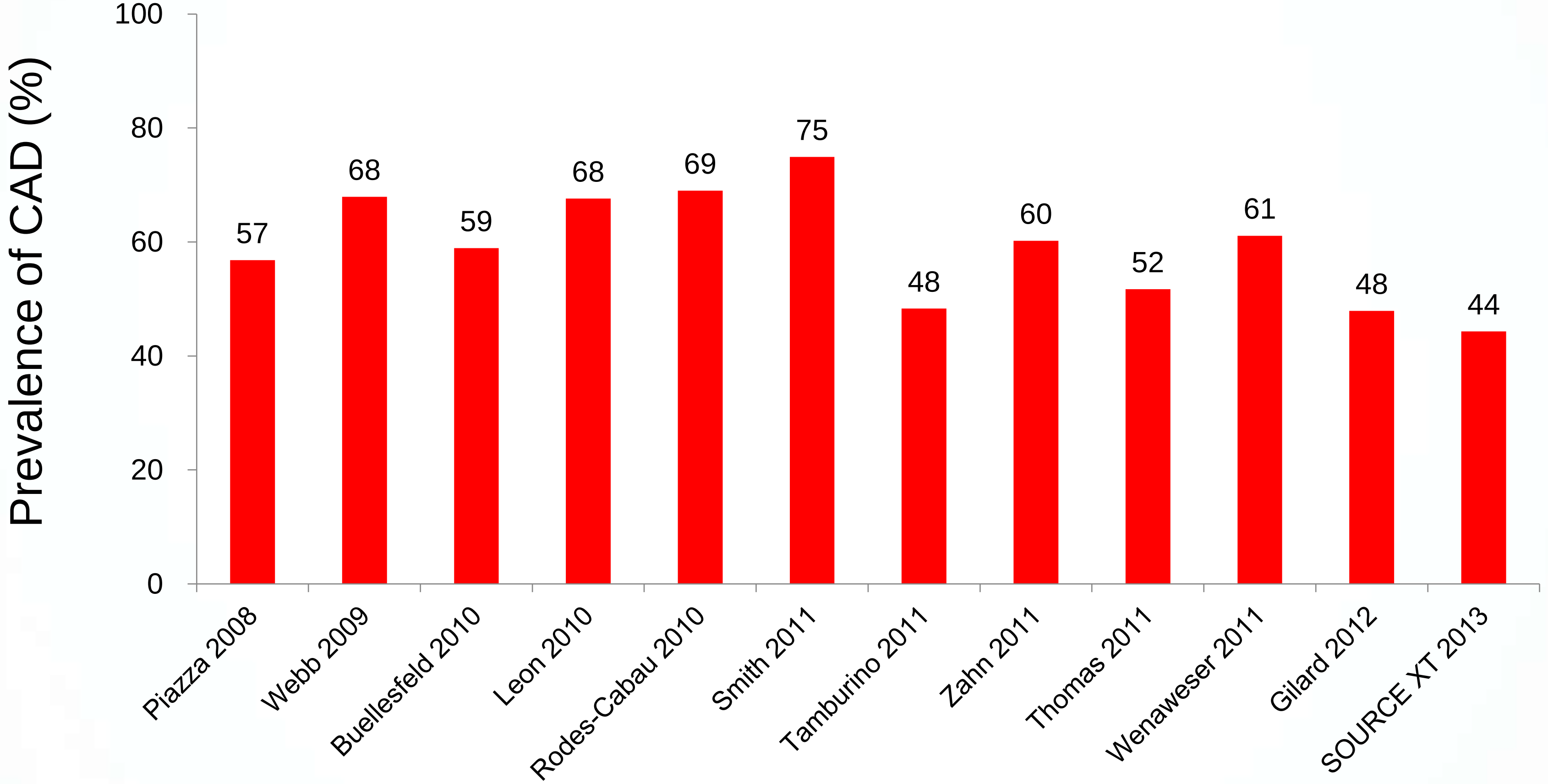
Milin AC et al, J Am Heart Assoc. 2014 Sep;5:e001111

Incidence of CAD in Severe AS



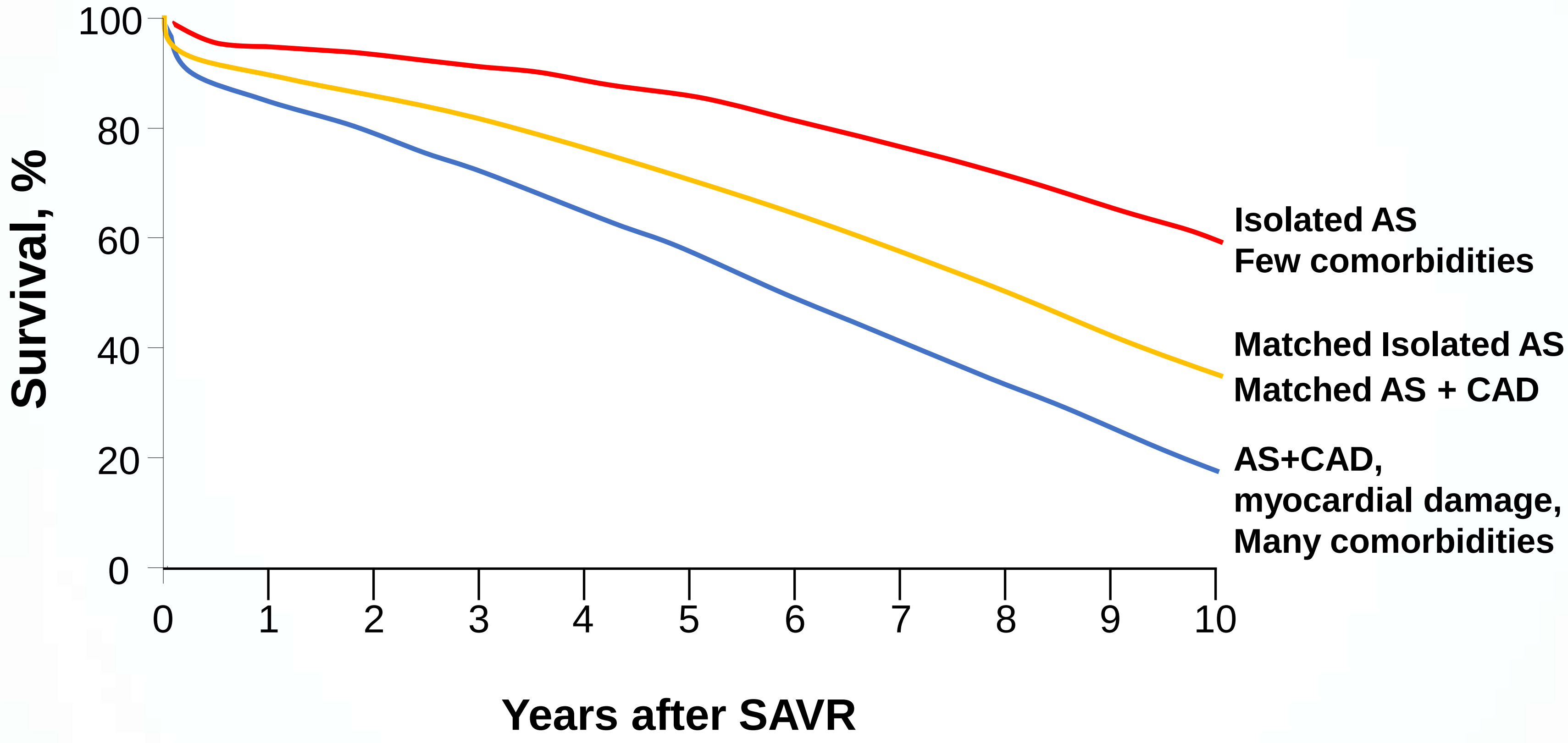
Stefanini GG et al, Eurointervention. 2013;9:S63-S68

Incidence of CAD in TAVR Patients



Impact of CAD on SAVR

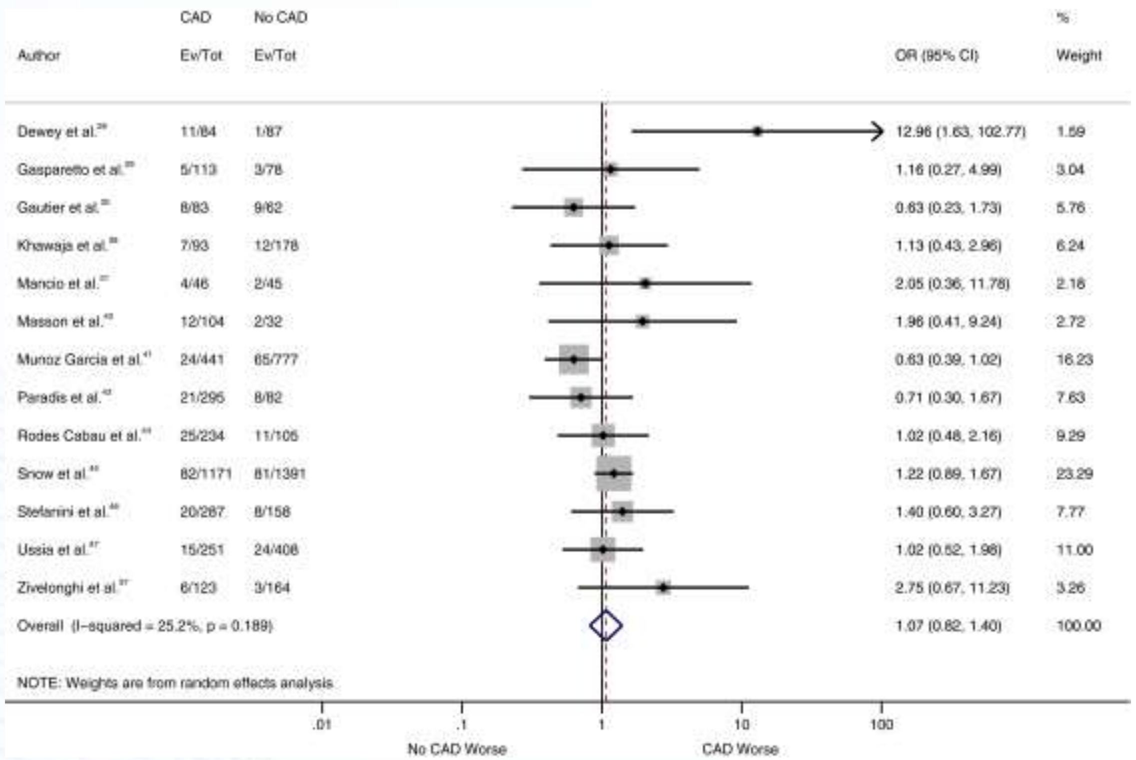
From 1991 to 2010, 2,286 patients with AVR+CABG versus 1,637 AVR alone from Cleveland Clinic



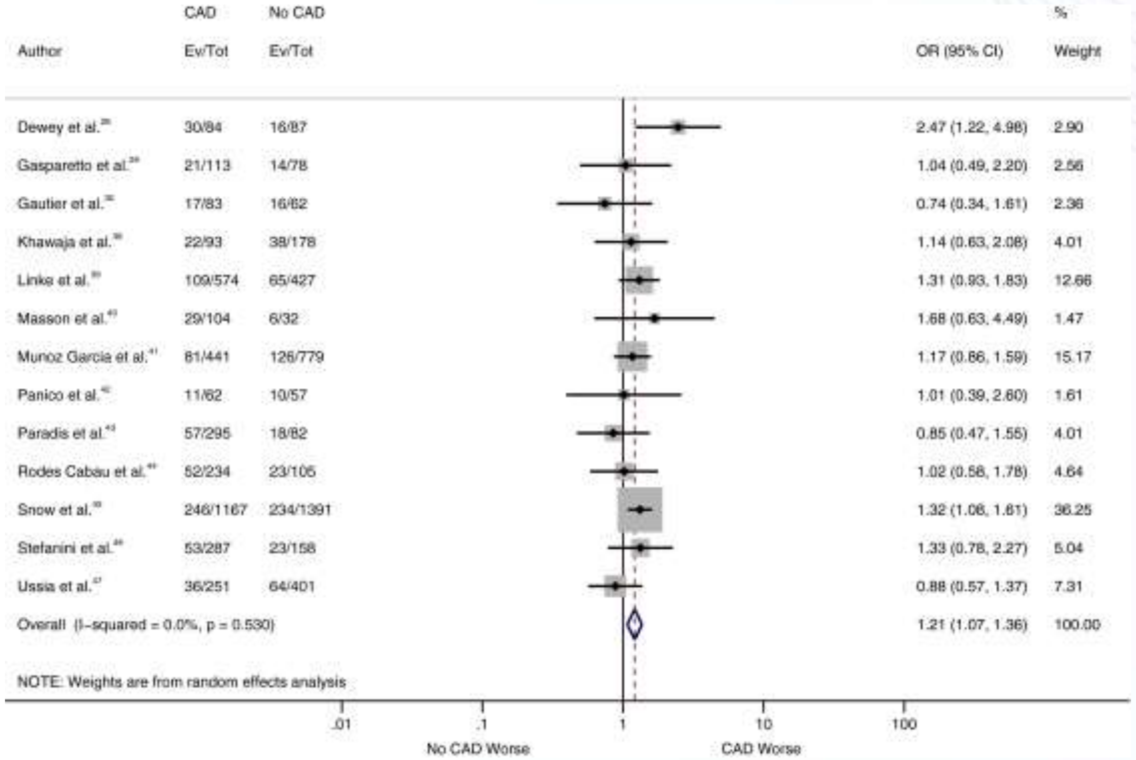
Impact of CAD on Mortality After TAVR

Meta-analysis: 8013 patients from 15 studies

30 Days Mortality



1 Year Mortality



J Am Heart Assoc. 2017;6:e006092

Impact of CAD on Mortality After TAVR

Meta-analysis: 8013 patients from 15 studies

Study	Mean Age, y	Men, %	STS (Mean)	EuroSCORE (Mean)	CAD, %	CAD Definition
Dewey et al[28]	83.8	49.1	12.06	30.86	49.1	Prior CABG/PCI
Gasparetto et al[29]	80.5	42.4	NA	21.4	59.2	Prior CABG/PCI and/or presence of any coronary stenosis of at least 50%
Gautier et al[30]	82	52.7	16	28	57.2	Prior CABG/PCI or >70% stenosis (>50% for left main)
Khawaja et al[38]	82.5	55.7	6.14	21.46	34.3	>70% stenosis (>50% for left main)
Linke et al[39]	81.1	49	5.3	16	57.3	Not specified
Mancio et al[31]	79	52	6	NA	50.6	Prior CABG/PCI and/or presence of any coronary stenosis of at least 50%
Masson et al[40]	85.1	50.7	9.1	21	30.3	Prior CABG/PCI or >50% stenosis (extent was assessed by DMJS)
Muñoz-García et al[41]	80.7	45.3	NA	17.8	36.[illegible]	Not specified
Panico et al[42]	82.5	46.6	NA	25.8	51.7	Not specified
Paradis et al[43]	82.5	51.9	8.5	25.4	78.2	>50% stenosis in vessels >1.5 mm in diameter
Rodés-Cabau et al[44]	81	44.8	9.8	NA	69	Not specified
Snow et al[45]	81.3	46.3	NA	18.06	45.7	>50% stenosis of the left main or 3 main coronaries or their major epicardial branches
Stefanini et al[46]	82.5	44	6.9	23.4	64.5	>50% stenosis in vessels ≥1.5 mm in diameter
Ussia et al[47]	81.2	40	NA	23.1	38.[illegible]	Prior CABG/PCI
Zivelonghi et al[37]	81.2	43.2	NA	28.6	42.9	>50% Stenosis

Nonuniformity in the CAD definitions used in RCTs, registries, and large observational studies and absence of stratified TAVR outcomes based on the CAD status of patients in RCTs and major registries.

J Am Heart Assoc. 2017;6:e006092

Guideline

ESC (DS>70%)

Recommendations for management of CAD in patients with VHD.

Recommendations	Class[a]	Level[b]
Indications for myocardial revascularization		
PCI should be considered in patients with a primary indication to undergo TAVI and coronary artery diameter stenosis >70% in proximal segments.	IIa	C

[e]Stenosis ≥50% can be considered for left main stenosis.
[f]FFR ≤0.8 is a useful cut-off indicating the need for an intervention in patients with mitral or tricuspid diseases, but has not been validated in patients with aortic stenosis.

ACC/AHA (DS>70%, FFR, iFR)

Recommendations for Management of CAD in Patients Undergoing TAVI
Referenced studies that support the recommendations are summarized in Online Data Supplement 45.

COR	LOE	RECOMMENDATIONS
1	C-EO	1. In patients undergoing TAVI, 1) contrast-enhanced coronary CT angiography (in patients with a low pretest probability for CAD) or 2) an invasive coronary angiogram is recommended to assess coronary anatomy and guide revascularization.
2a	C-LD	2. In patients undergoing TAVI with significant left main or proximal CAD with or without angina, revascularization by PCI before TAVI is reasonable (1,2).
2a	C-LD	3. In patients with significant AS and significant CAD (luminal reduction >70% diameter, fractional flow reserve <0.8, instantaneous wave-free ratio <0.89) consisting of complex bifurcation left main and/or multivessel CAD with a SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score >33, SAVR and CABG are reasonable and preferred over TAVI and PCI (3,4).

Randomized Trials on CAD Evaluation and Management in TAVR

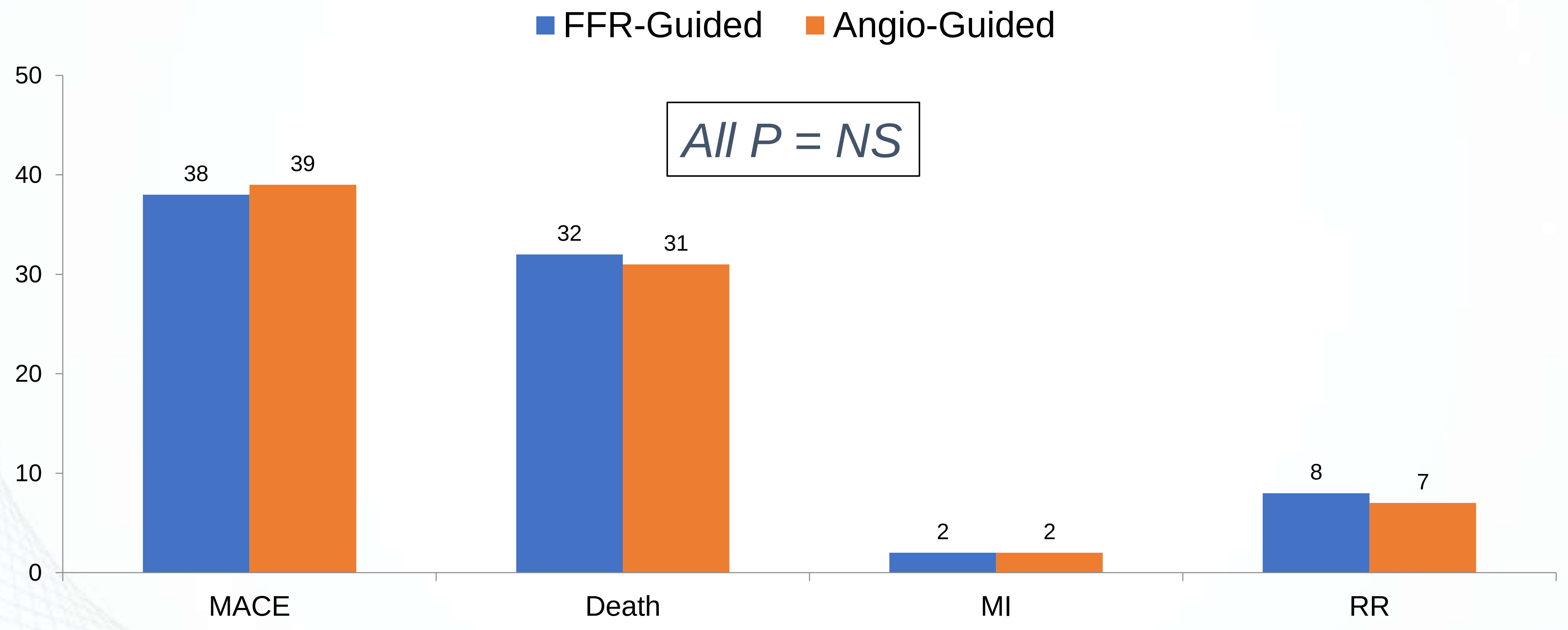
Study	Study Design	Population	Sample Size	Intervention	Primary Endpoint
CT-CA (NCT03291925)	Randomized open-label trial (pilot study)	Patients with symptomatic severe AS eligible for TAVR	200	Selective invasive angiography based on CT/coronary CTA imaging vs. systematic invasive angiography	Number of patients enrolled in the study of all those that are eligible
FORTUNA (NCT03665389)	Prospective open-label registry (exploratory)	Patients with moderate stenotic lesions (30%-<70%) or severe stenotic lesions on CTA who are candidates for PCI following TAVR	25	Measurement of iFR before TAVR, FFRct before TAVR and FFR + iFR after TAVR	FFRct before TAVR
TCW (NCT03424941)	Randomized open-label noninferiority trial	Patients age ≥70 yrs with severe AS feasible for treatment by both TF or TSc approach TAVR as well as conventional SAVR, and ≥2 de novo coronary lesions ≥50% diameter stenosis on main artery or side branch >2 mm or single LAD lesion >20 mm length or involving a bifurcation, feasible for treatment with CABG as well as PCI	328	FFR-guided PCI and TAVR vs. CABG and SAVR	Composite of all-cause mortality, myocardial infarction, disabling stroke, unscheduled clinically-driven target vessel revascularization, valve reintervention, and life threatening or disabling bleeding at 1 yr
FAITAVI (NCT03360591)	Randomized open-label trial	Patients with severe AS with the indication of TAVR and at least one coronary stenosis >50% at angiography	320	Physiologically-guided strategy (PCI of lesions with FFR ≤0.80) vs. angiographically guided strategy (PCI of all lesions >50% by visual estimation of major branches >2.5 mm)	Composite of all-cause death, myocardial infarction, stroke, major bleeding and target vessel revascularization at 1 yr
ACTIVATION (ISRCTN75836930)	Randomized trial	Patients with symptomatic severe AS accepted for TAVR, and ≥1 proximal stenosis of ≥70% in a major epicardial artery deemed suitable for PCI	310	Pre-TAVR PCI vs. no pre-TAVR PCI	Mortality and rehospitalization at 1 yr
NOTION-3 (NCT03058627)	Randomized open-label trial	Patients with severe aortic stenosis selected for TAVR and at least one coronary stenosis with FFR ≤0.80 or diameter stenosis >90% in a coronary artery ≥2.5 mm	452	TAVR only vs. TAVR + FFR-guided complete revascularization	All-cause mortality, myocardial infarction, or urgent revascularization at 1 yr

J Am Coll Cardiol 2019;74:362–72

Physiologic CAD Assessment

FFR guided PCI in AS

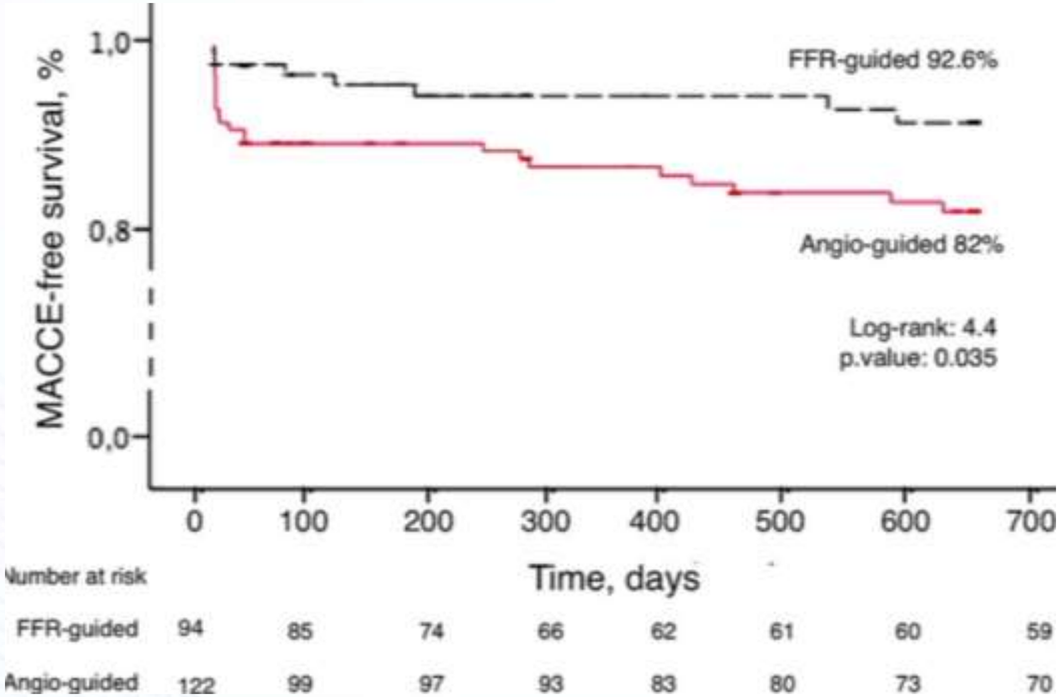
106 patients with AS (66% severe AS) and intermediate CAD under the FFR guidance versus 212 matched patients under the CAG guidance



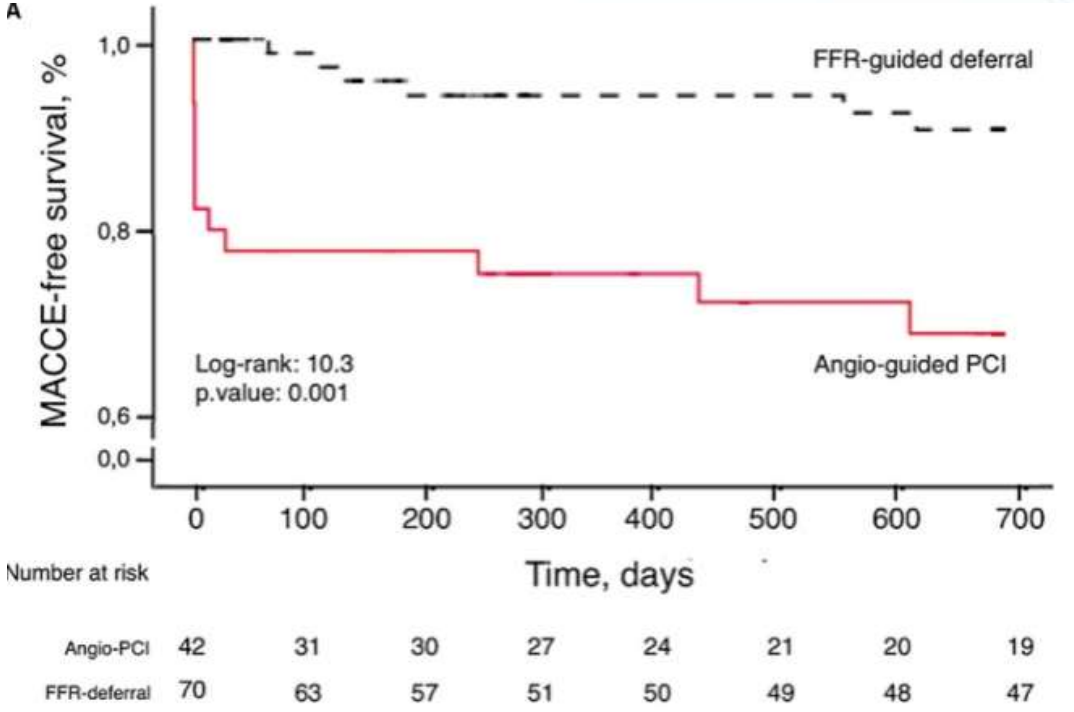
Di Gioia G et al. Am J Cardiol. 2016 May 1;117(9):1511-5

FFR guided Revascularization in Patients with TAVR

FFR guided Revascularization



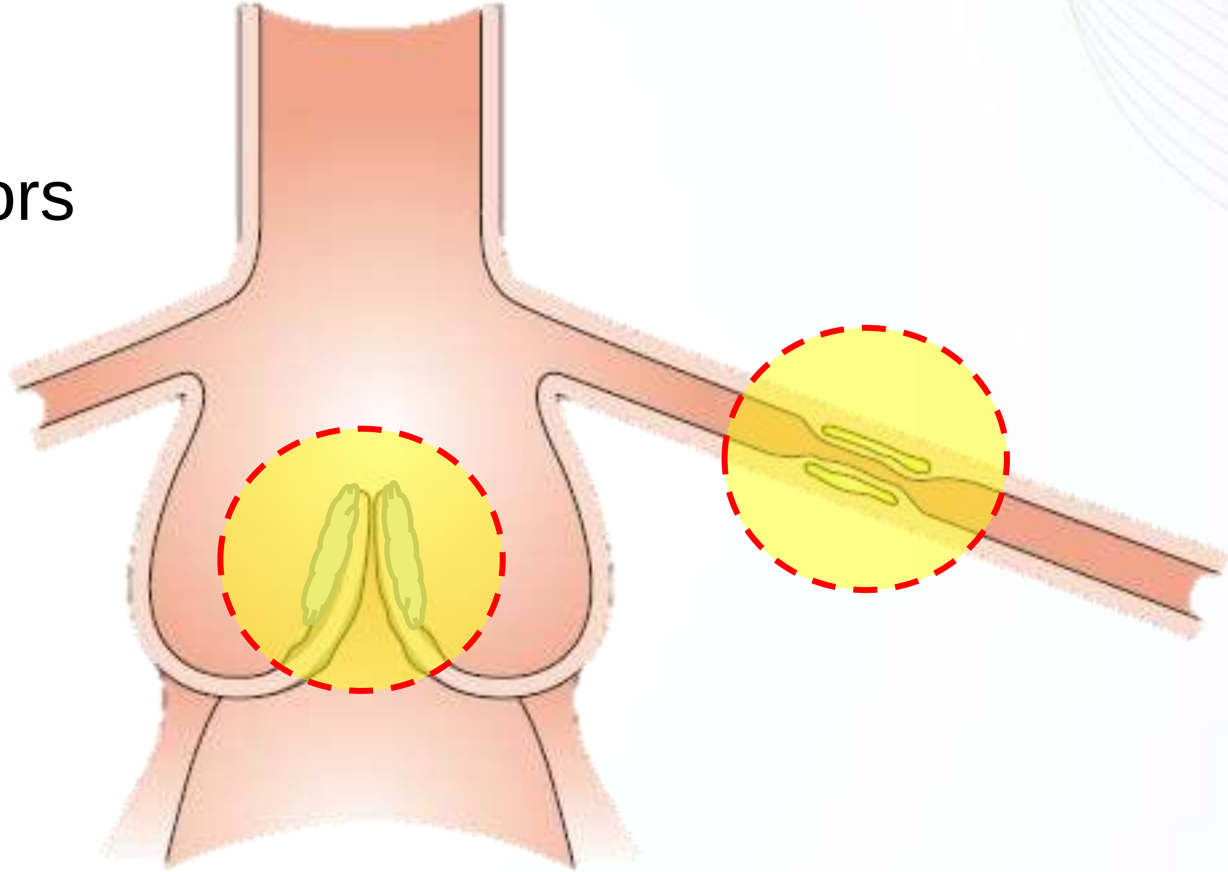
FFR guided Deferral



J Am Heart Assoc. 2019 Nov 19;8(22):e012618

Potential Problems with Physiology in AS

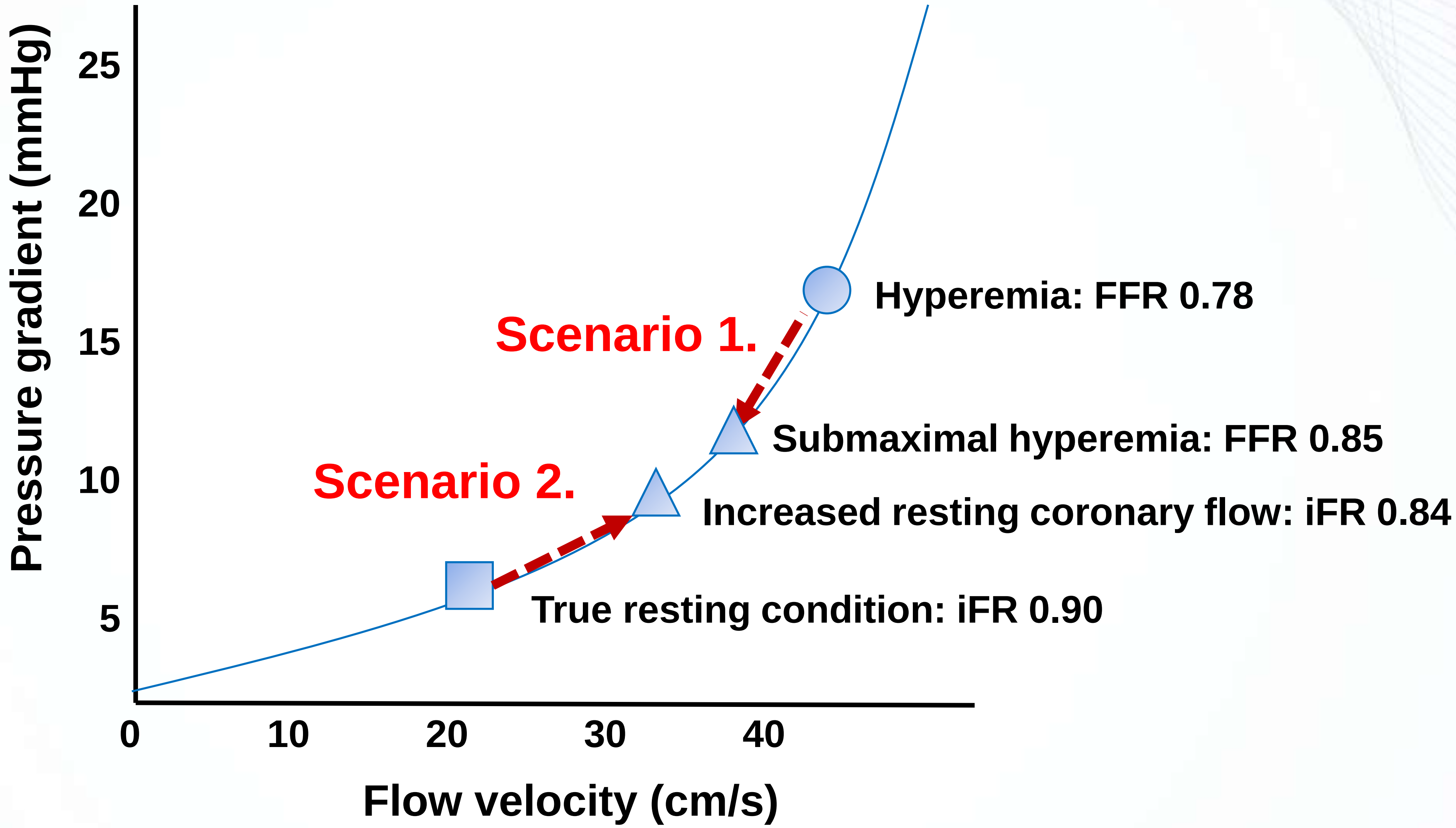
- Low CFR
- LVH
- Increased circulating vasoconstrictors
- Impaired maximal hyperemic flow
- Tandem effect



Circulation: Cardiovascular InterventionsVolume 12, Issue 8, 16 August 2019
https://doi.org/10.1161/CIRCINTERVENTIONS.118.007547

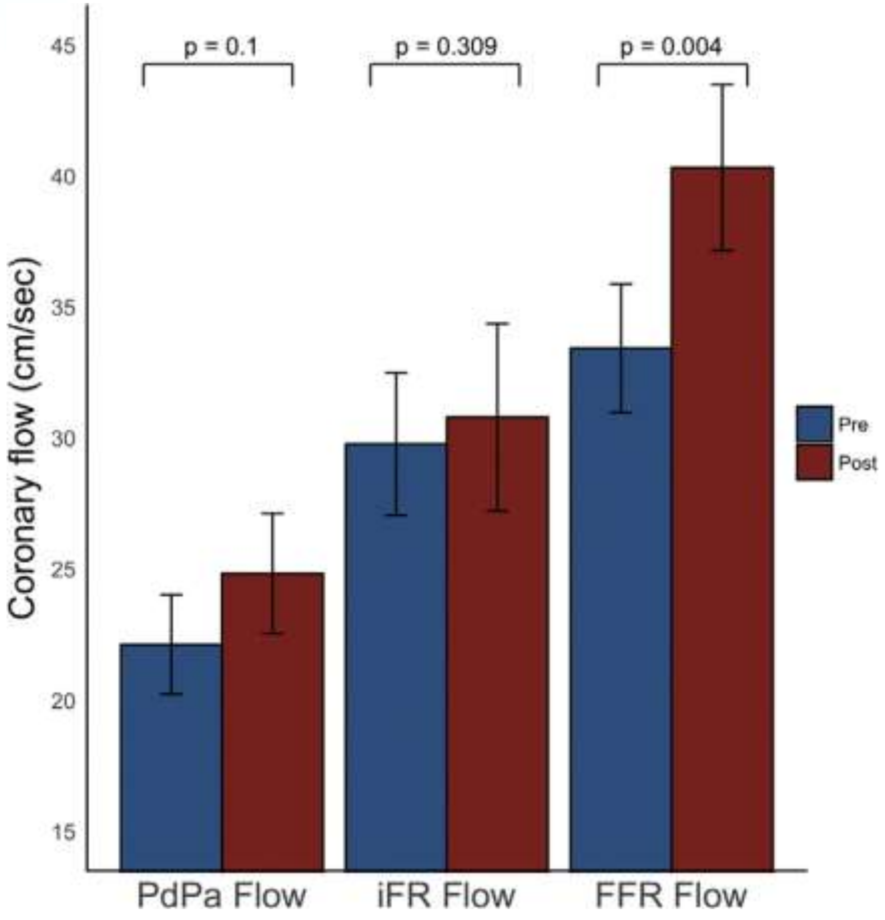
83 YO/Male with Severe AS

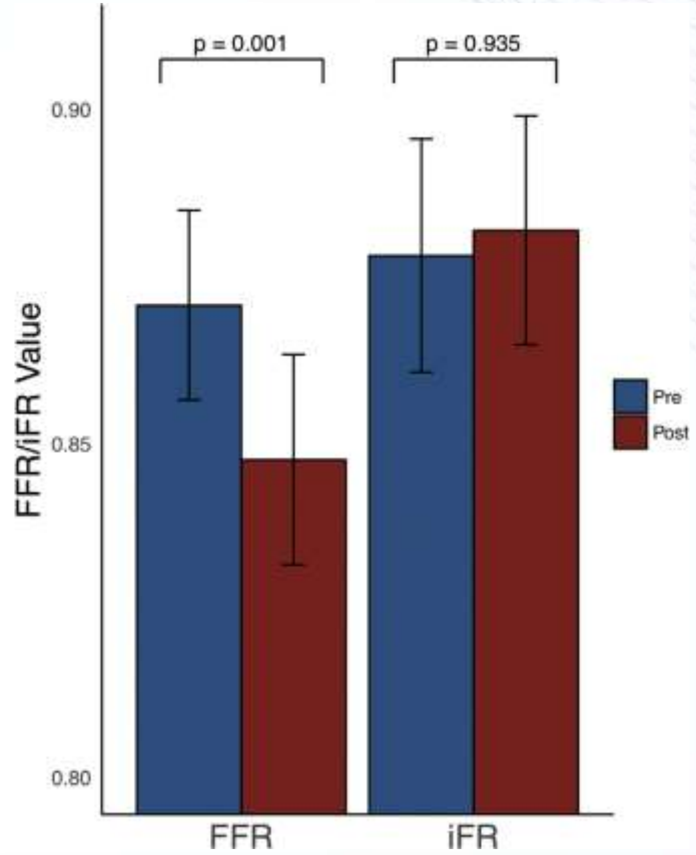
FFR and iFR Discordance in Severe AS



Changes in FFR and iFR After TAVR

- Patients with severe AS scheduled for TAVI
- Moderate to severe CAD on CAG
- 30 stenoses (28 patients) recruited from Imperial College London, UK and Skane University Hospital, Sweden





	Pre-TAVR	Post-TAVR	p Value
Hyperemic indices			
Fractional flow reserve	0.87 ± 0.08	0.85 ± 0.09	0.0008
Resting indices			
Instantaneous wave-free ratio	0.88 ± 0.09	0.88 ± 0.09	0.94

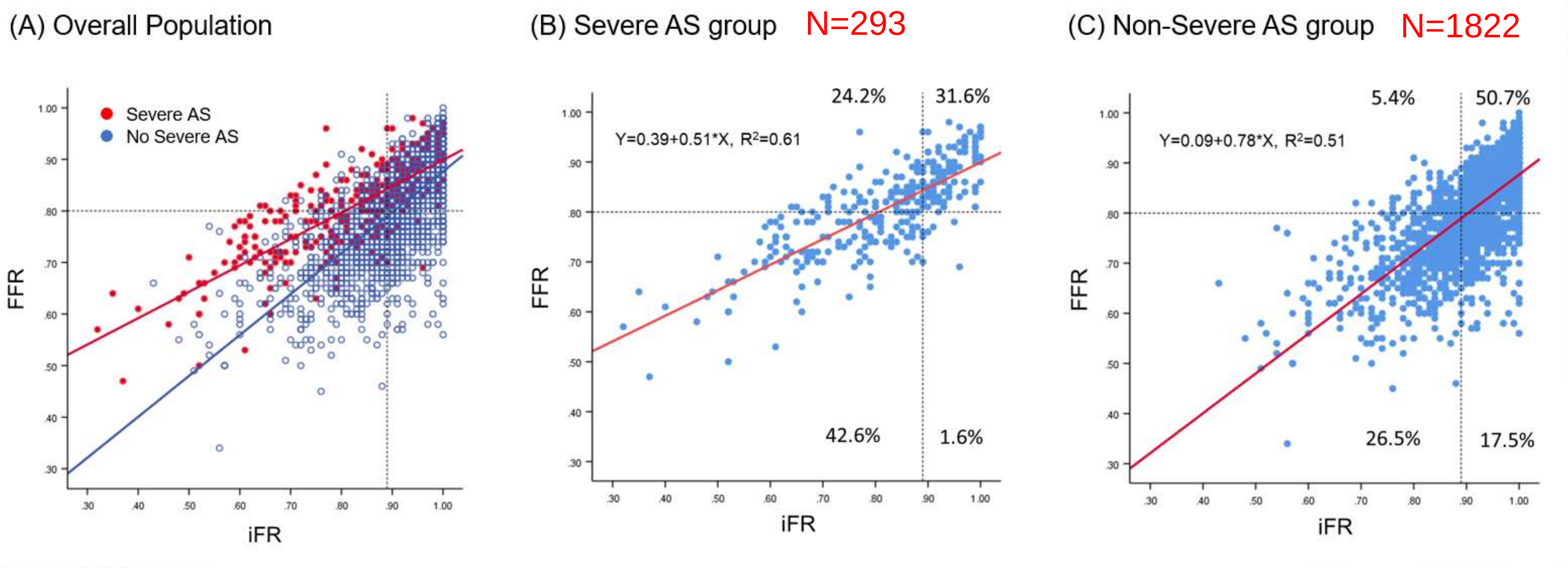
J Am Coll Cardiol Intv 2018;11:2019-31

Summary of Studies to Evaluate iFR and FFR in Severe AS

Author	Year (Ref.#)	Patients						
Mean or median*			iFR			FFR		
			Before TAVR	After TAVR	At Follow-up	Before TAVR	After TAVR	At Follow-up
Pesarini et al.	2016(16)	54				0.89±0.10	0.89±0.13	
Scarsini et al.	2017(12)	85	0.88±0.11			0.87±0.09		
Stoller et al.	2018(17)	40				0[illegible]3	0.93±0.08*	
Yamanaka et al.	2018(18)	95	0.86[illegible]93)			0.84[illegible]91)		
Ahmad et al.	2018(9)	28	0.[illegible]	0.88±0.09		0[illegible]3	0.85±0.09*	
Scarsini et al.	2018(11)	66	0.[illegible]	0.89±0.12		0[illegible]9	0.88±0.06	
Scarsini et al.	2019(13)	28	0.82[illegible]91)			0.81[illegible]88)		
Arashi et al.	2019(19)	13	0.[illegible]			0[illegible].		
Scarsini et al.	2019(14)	82				0[illegible].		
Vendrik et al.	2020(10)	13	0.82[illegible]90)	0.83 (0.77-0.88)	0.91 (0.84-0.94)	0.85[illegible]88)	0.79 (0.74-0.83) †	0.71 (0.65-0.77)†
Scarsini et al.	2020(15)	14	0.87[illegible]92)	0.88 (0.83-0.92)	0.88 (0.82-0.92)	0.88[illegible]96)	0.90 (0.83-0.93)	0.91 (0.86-0.97)
Stundl et al.	2020(20)	12				0[illegible]4	0.76±0.08	
Sabbah et al.§	2022(21)	32	0.[illegible])		0.92 (0.83-0.95)†	0[illegible])		0.86 (0.78-0.90)
Yamanaka et al.	2023(22)	140	0.85 ([illegible].91)			0.84 ([illegible].88)		

Significant iFR ***Insignificant iFR***

IRIS-FFR Registry

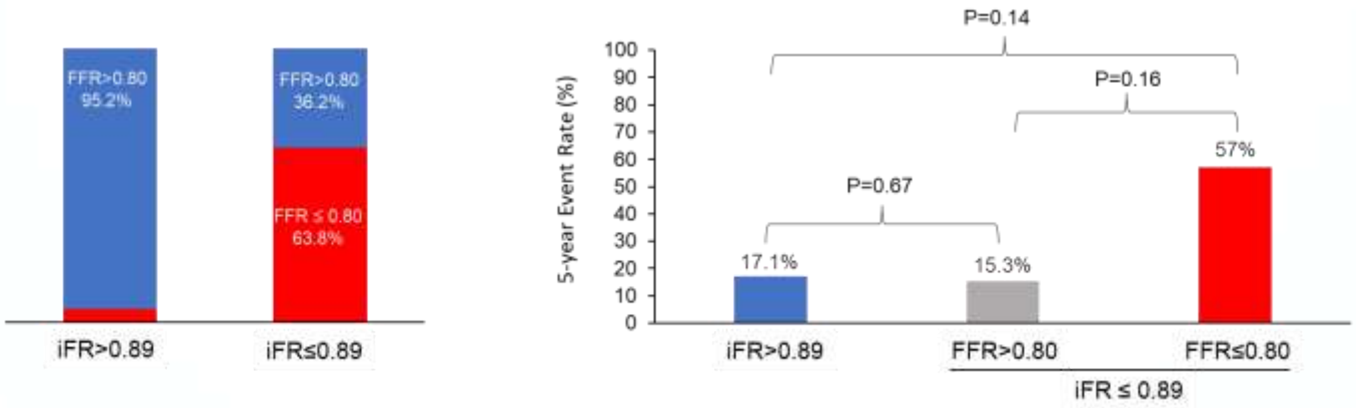


Circulation Cardiovascular Intervention in Submission

IRIS-FFR Registry

Incidence of Hemodynamically Significant Stenosis in Severe AS Group and No Severe AS Group

Prognostic Value of iFR and FFR in Severe AS Group



Circulation Cardiovascular Intervention in Submission

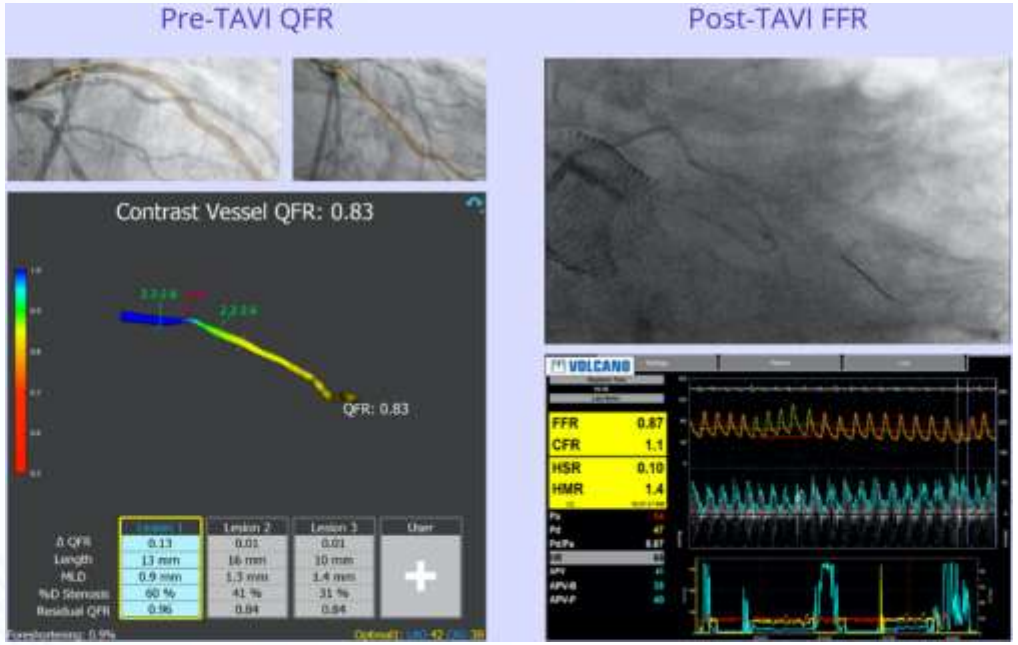
83 YO/Male with Severe AS

Physiologic CAD Assessment in Severe AS

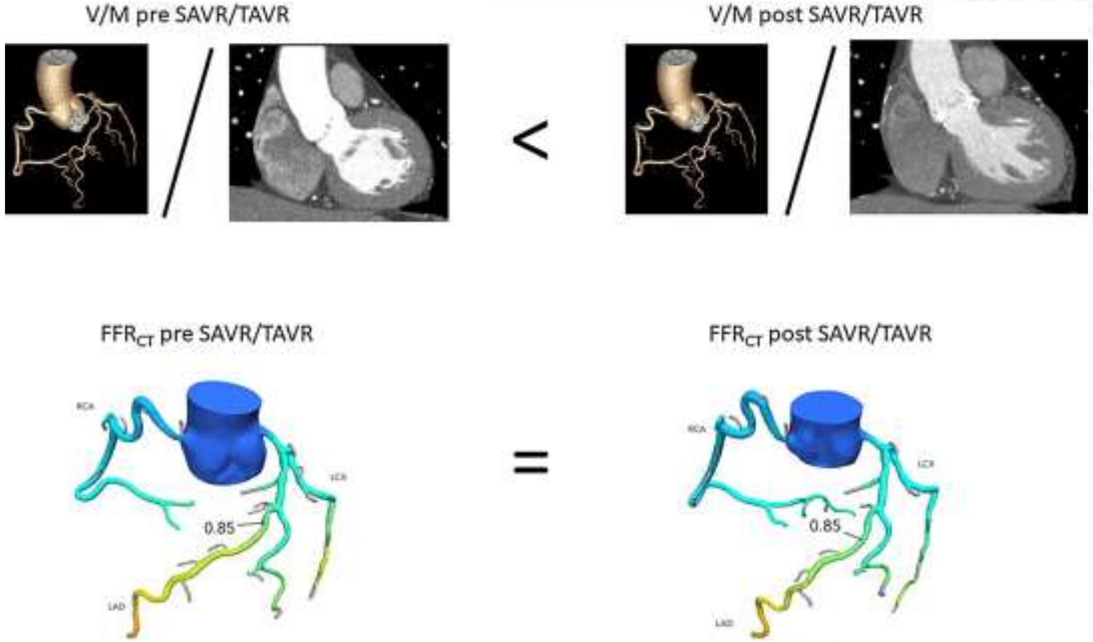
- FFR appeared to be less affected by the presence of severe AS.
- iFR may overestimate the functional severity of coronary artery disease without providing prognostic significance.

Circulation Cardiovascular Intervention in Submission

Simulated FFR



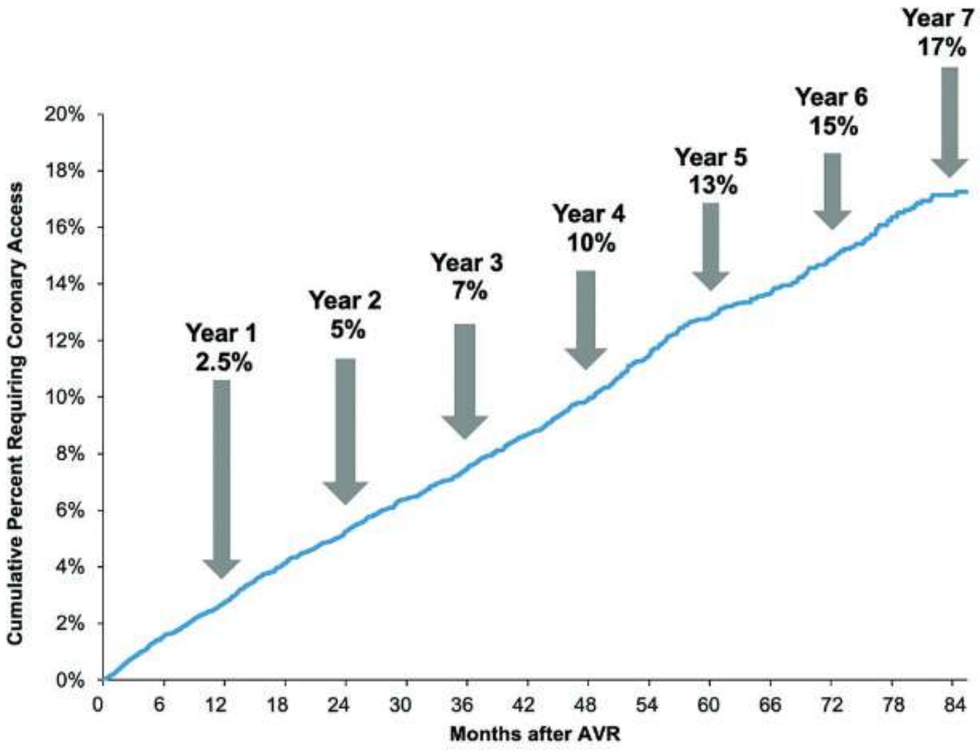
Catheter Cardiovasc Interv. 2022 Jan 1;99(1):68-73

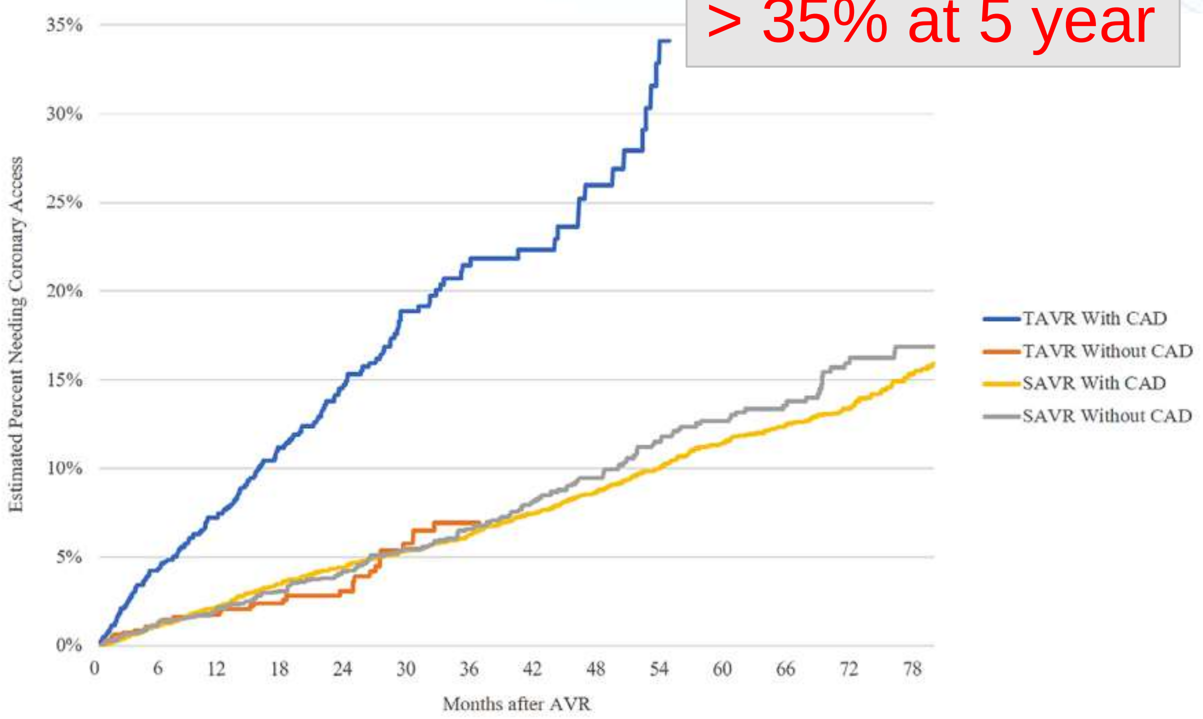


Int J Cardiovasc Imaging. 2022 Feb;38(2):427-434

Coronary Access After TAVR

The Need for Future Coronary Access after TAVR or SAVR

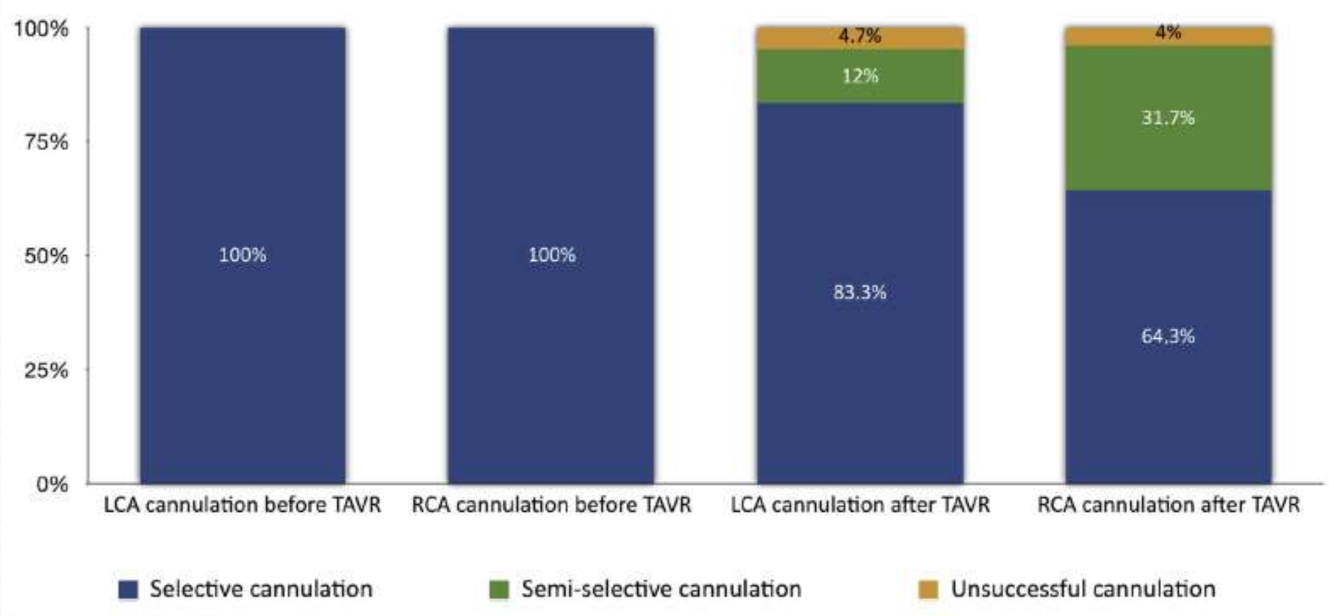




> 35% at 5 year

Catheter Cardiovasc Interv.2021;98:950–956

Coronary Access after TAVR
RE-ACCESS Single-Center Registry (N=300)



Transcatheter Aortic Valve/ Sinuses of Valsalva Relation
Odds Ratio 1.1;
95% CI: 1.0-1.2; p < 0.01

Transcatheter Aortic Valve Implant Depth
Odds Ratio 1.7;
95% CI: 1.3-2.3; p < 0.01

Evolut Transcatheter Aortic Valve
Odds Ratio 29.6;
95% CI: 2.6-335.0; p < 0.01

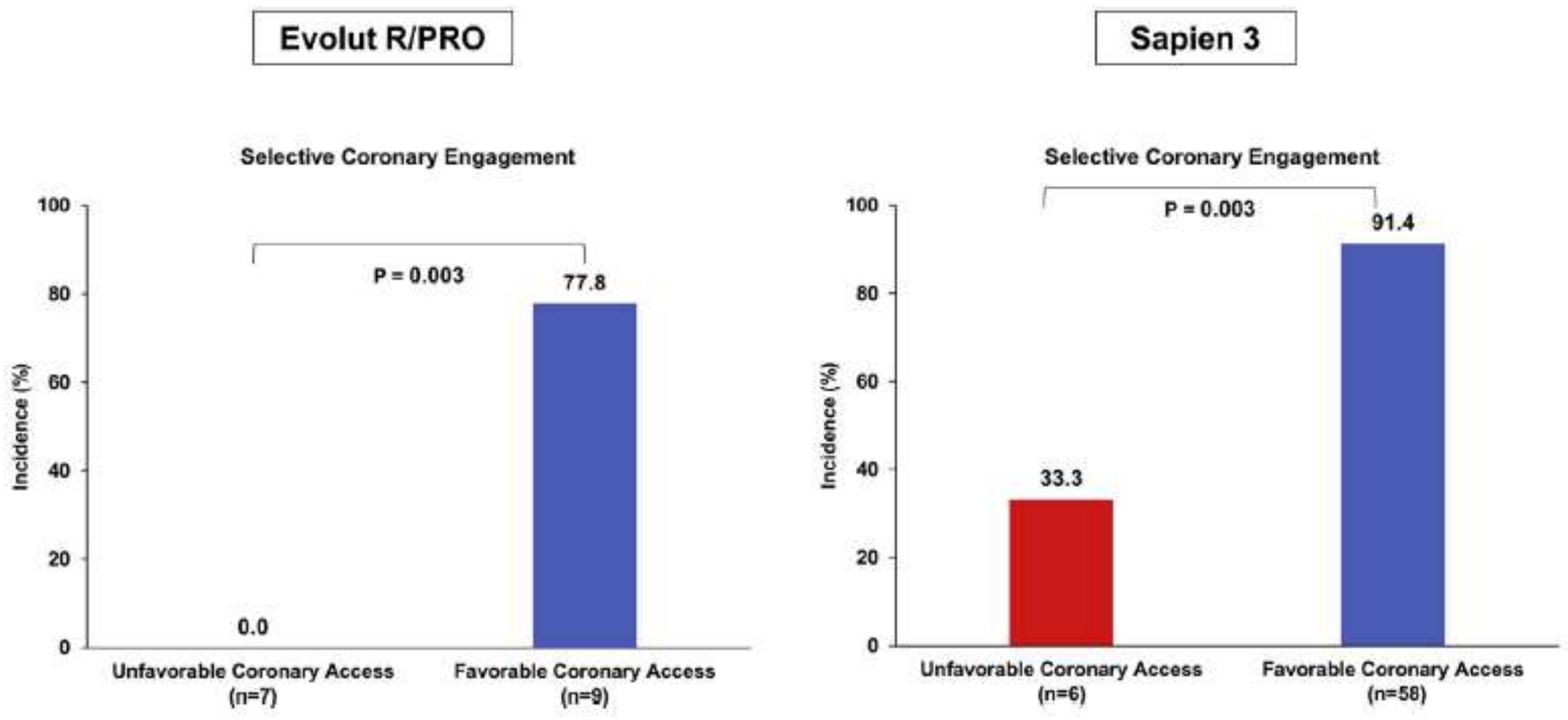
Barbanti M et al. J Am Coll Cardiol Intv. 2020;13:2542-55.

Coronary Access after TAVR : Feasible ~95% Cases

First Author, Year (Ref. #)	Population	Devices and Results	Conclusions
Blumenstein et al., 2015 (58)	35 patients who underwent CA or PCI after TAVR	Sapien XT: 19 of 19 selective CA; 8 of 8 successful PCI CoreValve: 3 of 10 selective CA, 6 of 10 nonselective CA, 1 of 10 nondiagnostic CA; no PCI Symetis: 2 of 4 selective CA, 2 of 4 nonselective CA; 1 of 1 successful PCI Jena: 1 of 1 selective CA; no PCI Portico: 1 of 1 nonselective CA; 1 of 1 successful PCI	Selective CA and PCI in patients with prior TAVR is generally feasible. Depending on stent frame type, the procedure can be challenging or even unfeasible.
Allali et al., 2016 (59)	24 PCI procedures in 17 patients with CoreValve bioprosthesis	4 of 24: difficult ostium intubation and suboptimal stability 23 of 24 procedural success (1 procedural death)	PCI after implantation of the self-expanding CoreValve is mostly feasible and safe. Selective intubation of the native coronary may be challenging.
Chakravarty et al., 2016 (38)	9 LM PCI: 4 patients with CoreValve and 5 with Edwards	9 of 9 successful PCI	LM PCI was feasible with self-expandable and balloon expandable TAVR bioprosthesis.
Chetcuti et al., 2016 (60)	190 CA and 113 attempted PCI in 169 patients with CoreValve bioprosthesis	186 of 190 successful CA 103 of 113 successful PCI	CA and PCI are possible in nearly all patients with CoreValve bioprosthesis.
Zivelonghi et al., 2016 (61)	66 patients who underwent CA or PCI after TAVR	Evolut R: 24 of 25 successful CA (of which 4 semiselective) and 6 of 6 successful PCI Sapien 3: 41 of 41 successful CA (of which 2 semiselective) and 13 of 13 successful PCI	Catheterization of the coronary ostia after TAVR with balloon or self-expandable valves is safe and feasible in almost all cases.
Boukantar et al., 2017 (62)	16 patients with CoreValve	9 of 16 adequate coronary opacification 6 of 7 successful PCI	CA after CoreValve TAVR are feasible but challenging.
Htun et al., 2017 (63)	43 CA in 28 patients with CoreValve or Evolut R	42 of 43 selective LMCA engagement 29 of 32 selective RCA engagement 29 of 29 successful PCI	CA and PCI after TAVR are feasible and safe with supra-annular self-expandable valve.
Tanaka et al., 2019 (64)	40 patients with CoreValve or Evolut R	16 of 32 RCA angiography success 28 of 32 LCA angiography success 28 of 30 PCI success	CA and PCI following CoreValve TAVR is safe and feasible in most cases. Success rate of selective RCA angiography is relatively low.

Faroux L et al., JACC 2019;74:362-72

Unfavorable Coronary Access After TAVR Can be Identified by CT



Ochiai T et al. J Am Coll Cardiol Intv. 2020;13(6):693–705.

Timing of PCI

Timing of PCI

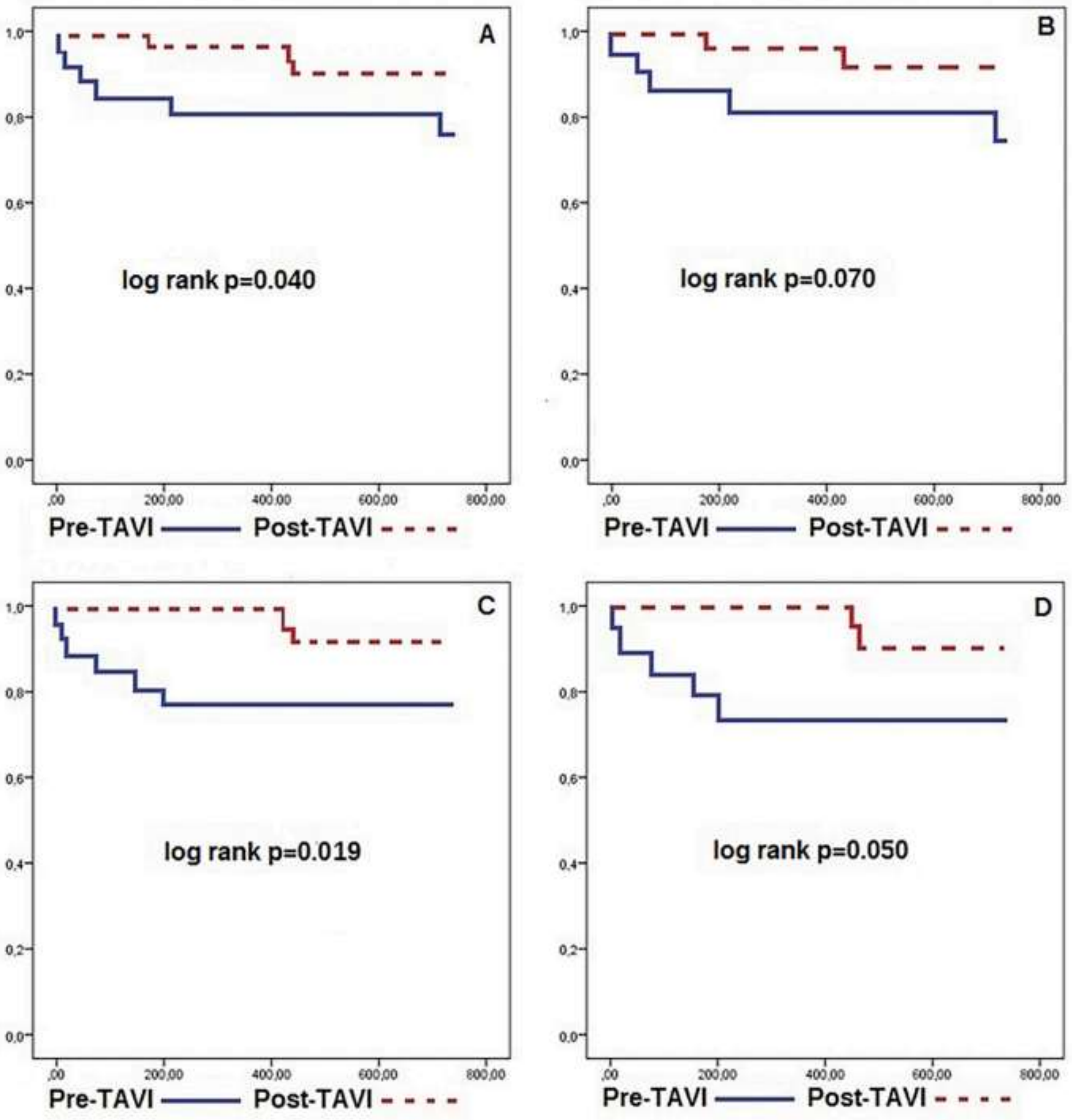
	pre-TAVI PCI	during-TAVI PCI	post-TAVI PCI
Pros	- possible lower risk of coronary events during TAVI procedure	- no need for additional vascular access	- more reliable physiological assessment of borderline lesions - reduced risk of stroke - possible lower risk of bleeding related to lack of pre-TAVI dual antiplatelet therapy
Cons	- risk of hemodynamic collapse during high-risk PCI procedures - increased bleeding risk	- higher contrast media load - additional costs	- difficult access to coronary ostia

International Journal of Cardiology 371 (2023) 128–129

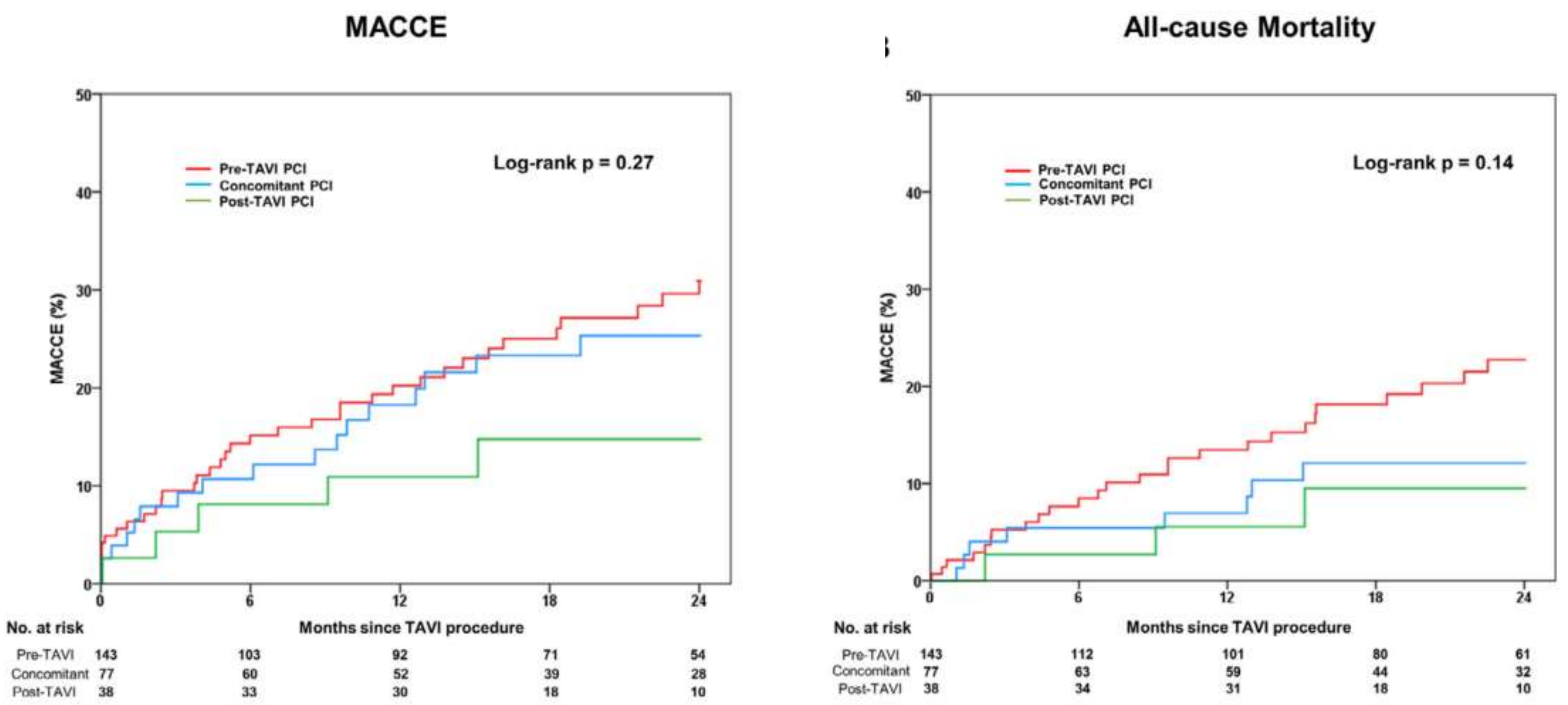
Overall PCI | High Risk PCI

Survival

MACCE



International Journal of Cardiology 365 (2022) 114–122

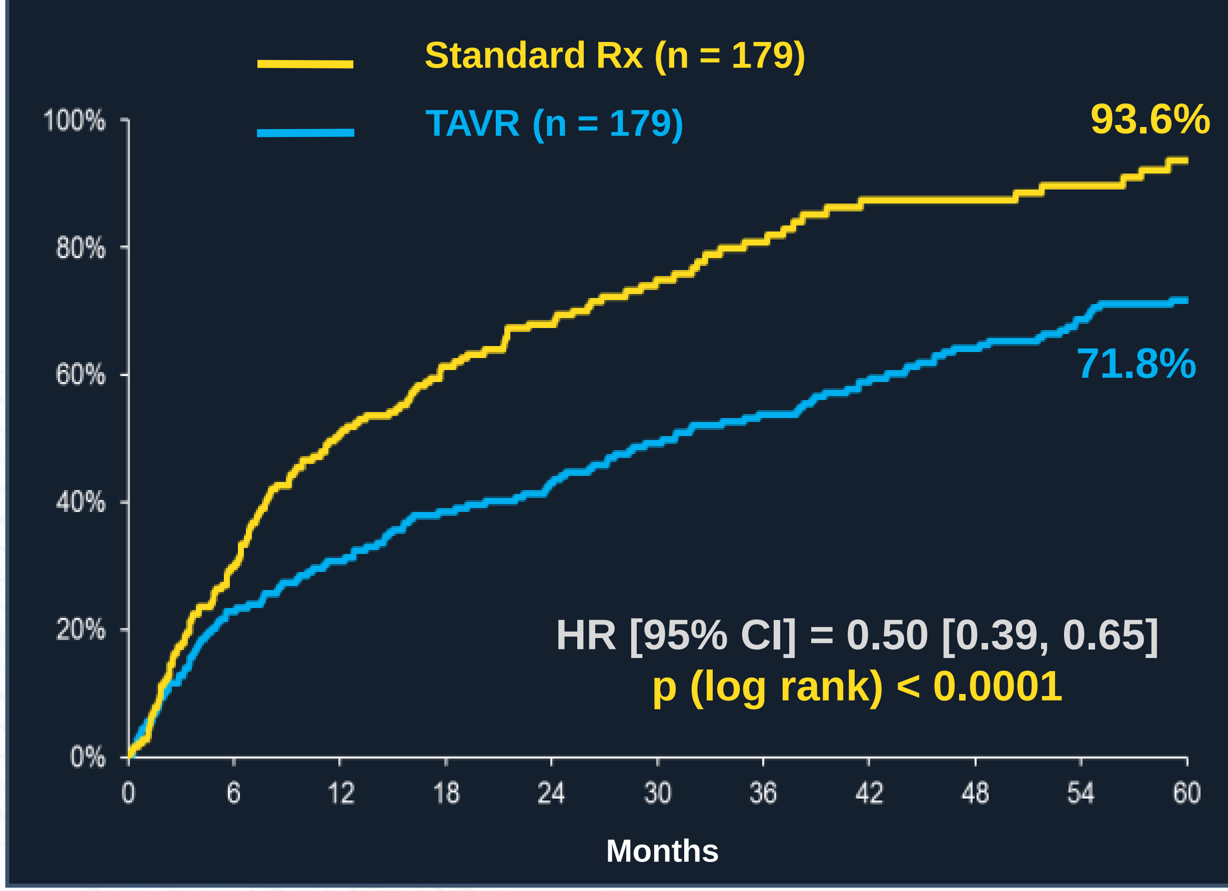


Am J Cardiol 2020;125:1361−1368

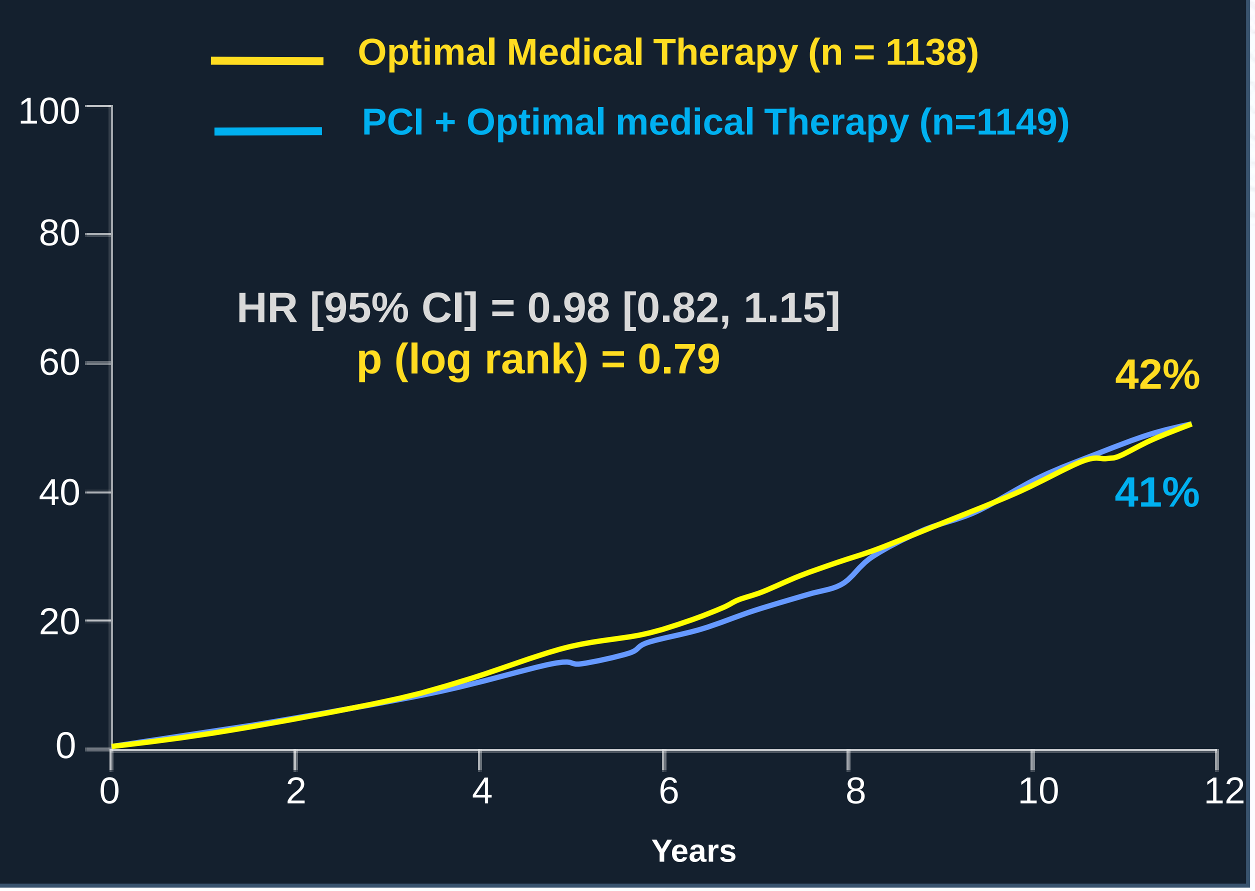
Concept of CAD Management in Severe AS

Mortality

PARTNER IB
- 5 YR mortality -



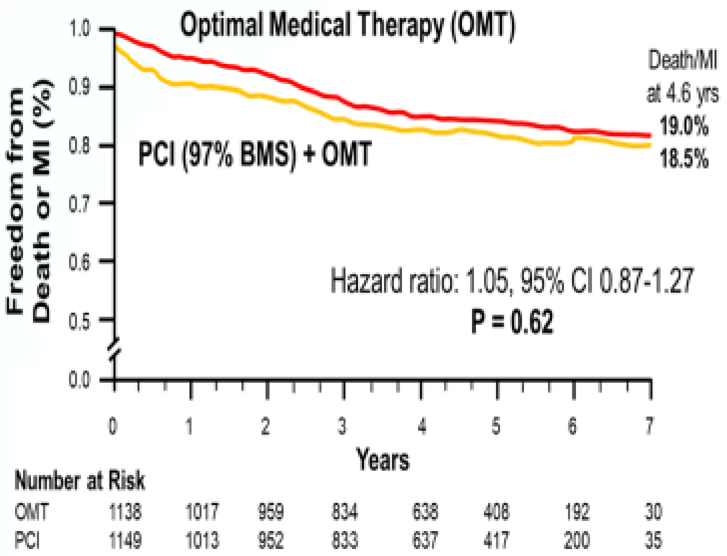
COURAGE
- 10 YR mortality -



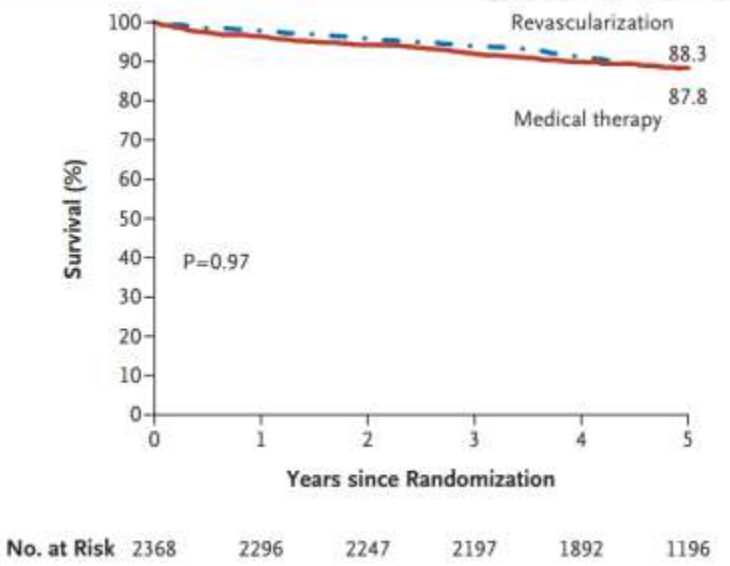
Kapadia SR et al, Lancet. 2015;385(9986):2485-91
Sedlis SP et al, NEJM. 2015;373:1937-46

Coronary Revascularization Did Not Improve The Survival Over OMT

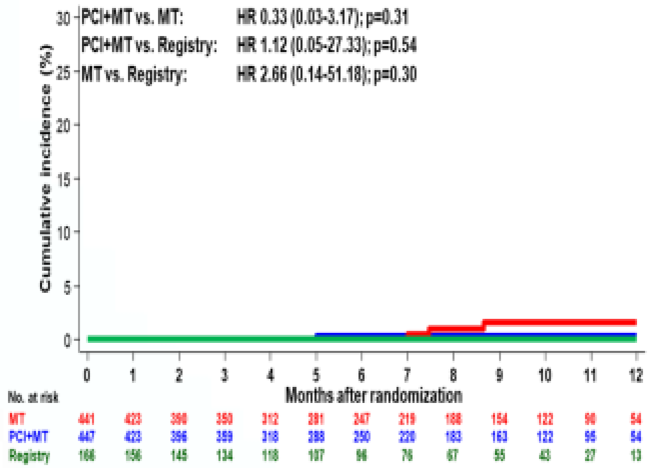
COURAGE



BARI2D



FAME II



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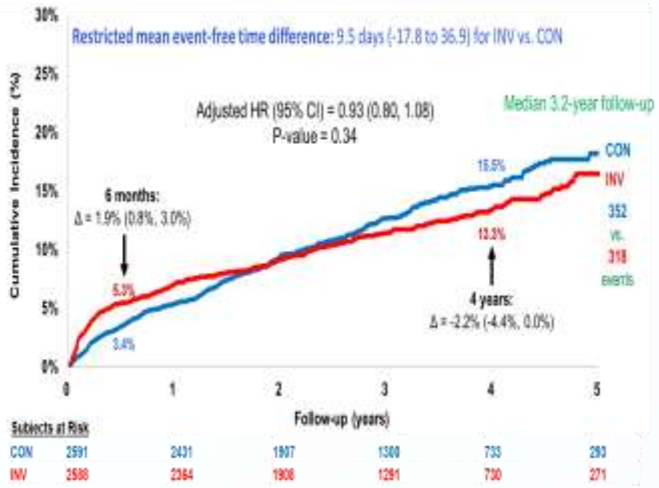


Reasonable Incomplete Revascularization: Revisited

Reasonable Incomplete Revascularization

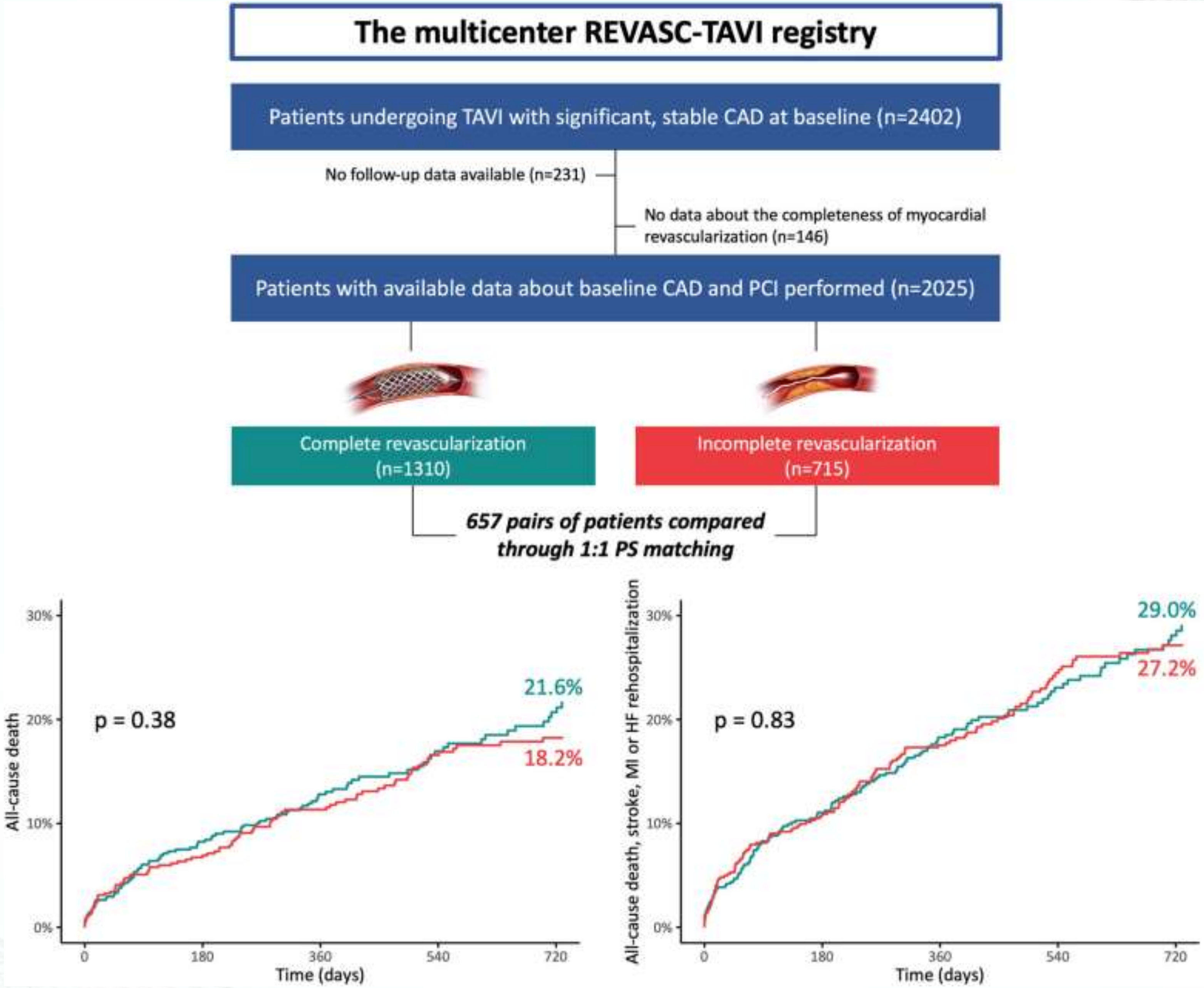
Focus on the proximal stenosis supplying large myocardium based on the physiologic guidance:
e.g. Left Main or proximal LAD

- Very small vessels
- Only 1-vessel IR
- Jailed asymptomatic side branch
- Not culprit artery (thrombus)

- Non-viable myocardium
- < 5% residual ischemic area expected
- Small ischemic area

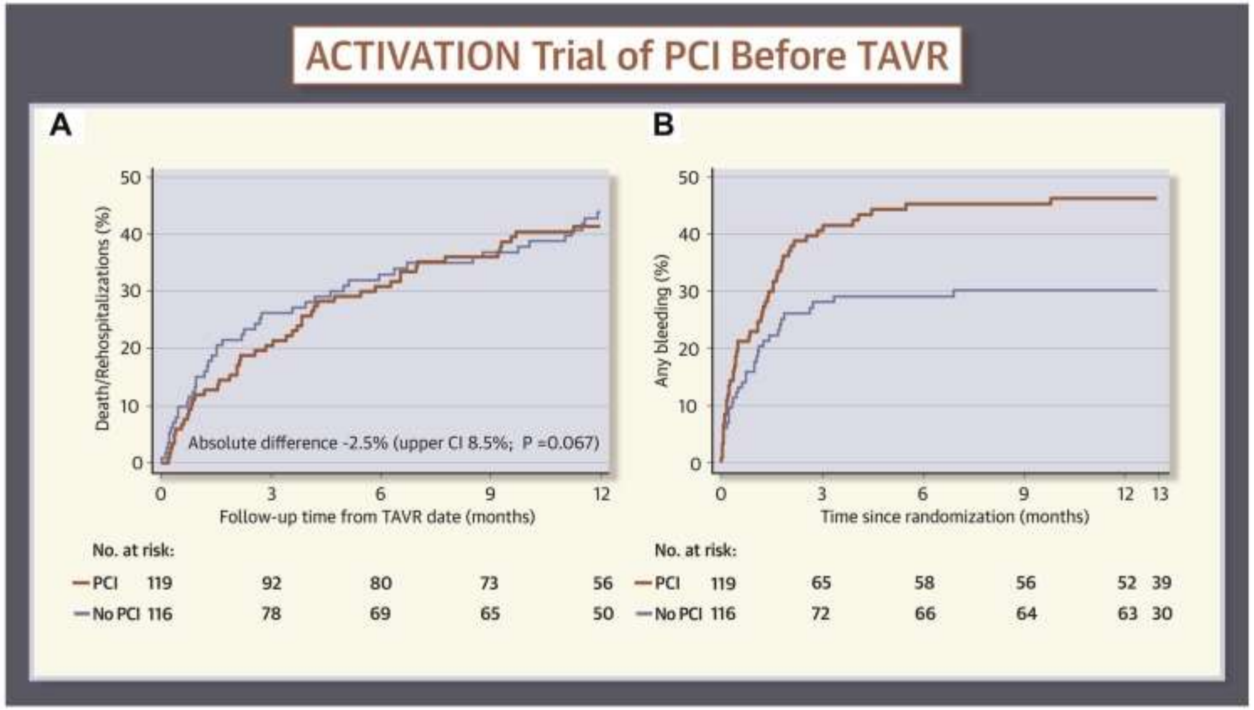
- FFR > 0.80

Dauerman HL. Circulation. 2011;123:2337


The multicenter REVASC-TAVI registry
Patients undergoing TAVI with significant, stable CAD at baseline (n=2402)
No follow-up data available (n=231)
No data about the completeness of myocardial revascularization (n=146)
Patients with available data about baseline CAD and PCI performed (n=2025)
Complete revascularization (n=1310)
Incomplete revascularization (n=715)
657 pairs of patients compared through 1:1 PS matching
All-cause death
p = 0.38
21.6%
18.2%
30%
20%
10%
0%
0
180
360
540
720
Time (days)
All-cause death, stroke, MI or HF rehospitalization
p = 0.83
29.0%
27.2%
30%
20%
10%
0%
0
180
360
540
720
Time (days)

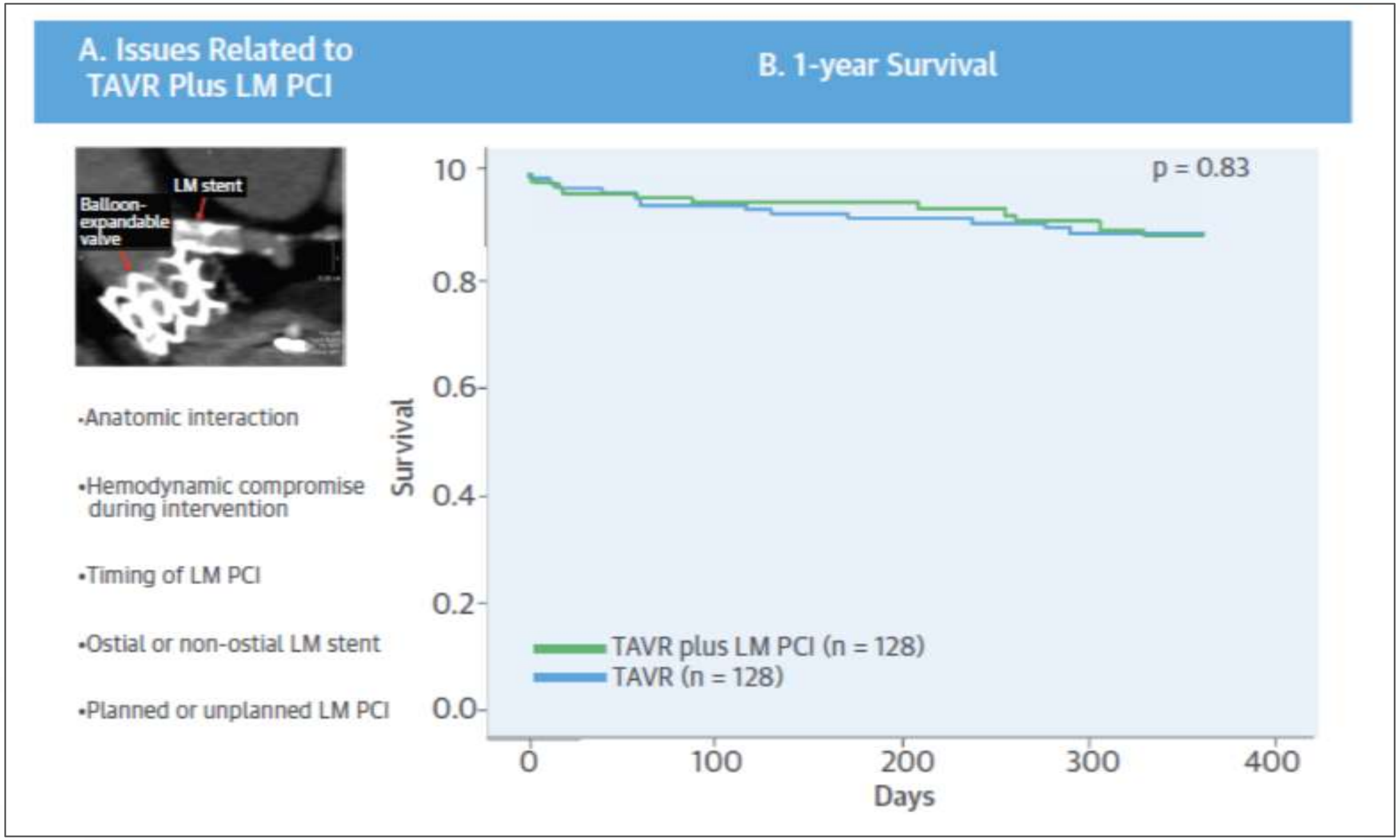
ACTIVATION Trial (N=235)

CENTRAL ILLUSTRATION: The ACTIVATION Trial of PCI Compared With No PCI Prior to TAVR Demonstrated No Difference in the Primary Endpoint of Death or Rehospitalization at 1 Year and Increased Bleeding Events in the PCI Arm



Patterson, T. et al. J Am Coll Cardiol Intv. 2021;14(18):1965-1974.

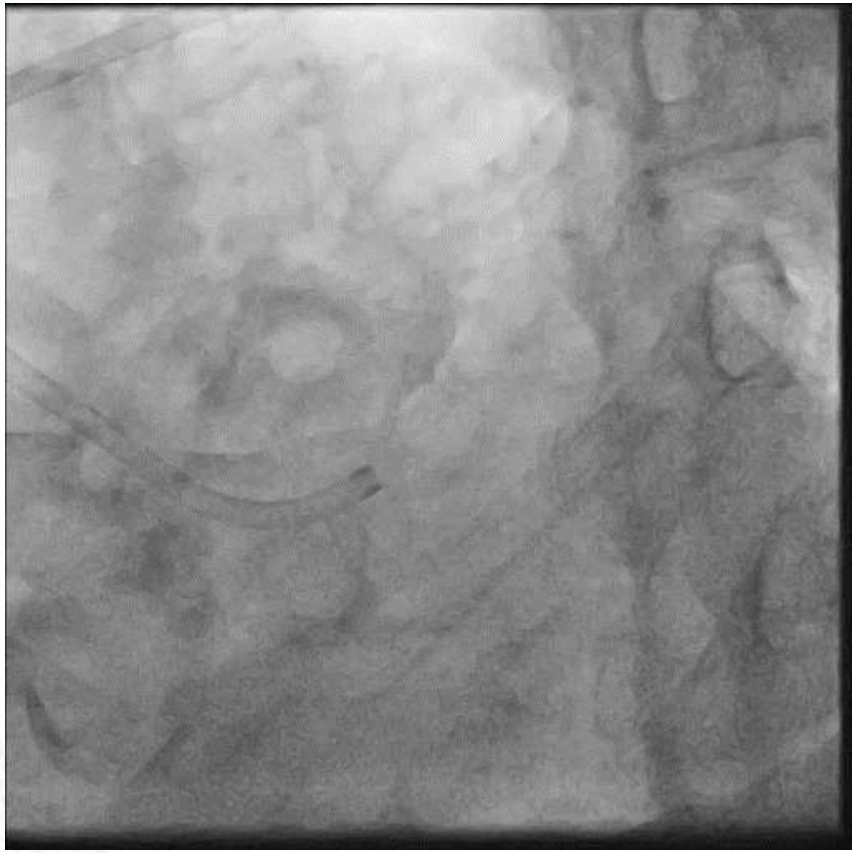
LM PCI in Severe AS

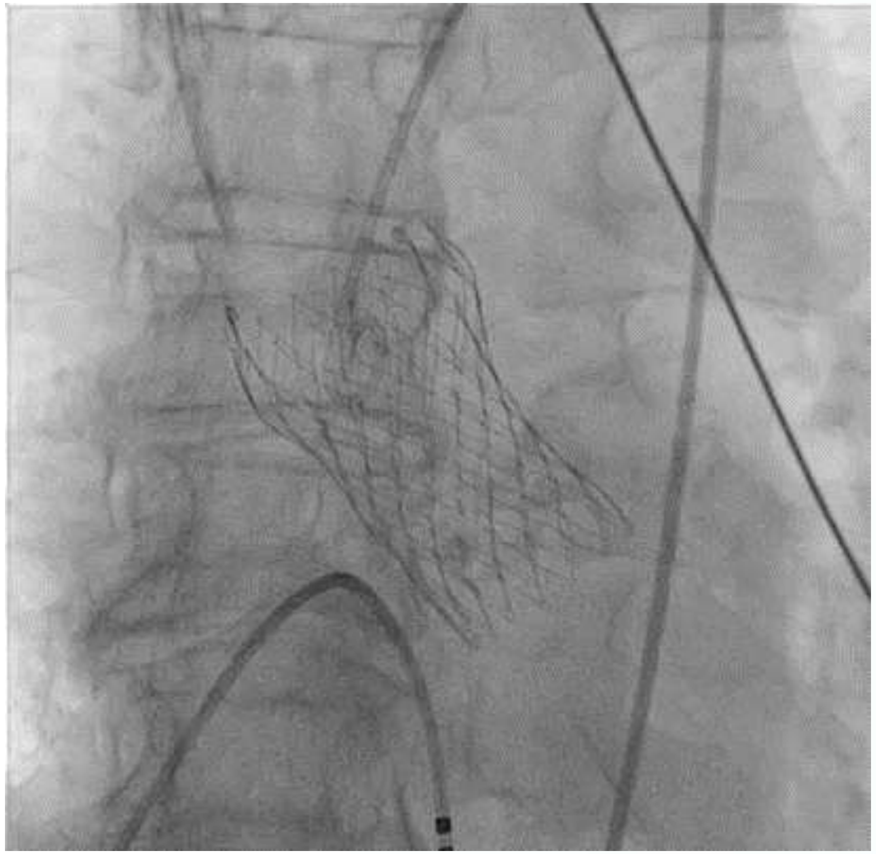


Chakravarty, T. et al. J Am Coll Cardiol. 2016; 67(8):951–60.

M/91 with Chest Pain

Severe AS and Severe CAD





How Can We Treat Patients with Concomitant Coronary Artery Disease?

- Degenerative aortic stenosis (AS) and coronary artery disease (CAD) share common pathophysiology and risk factors. Between 30-70% of patients undergoing surgical aortic valve replacement have significant CAD.
- Given the survival benefit of transcatheter aortic valve replacement (TAVR), relieving AS is often more important than coronary revascularization. A reasonable incomplete revascularize strategy appears to be appropriate for managing CAD in severe AS.
- Fractional flow reserve (FFR) appears to be less affected by the presence of severe AS, but instantaneous wave-free ratio (iFR) may overestimate the functional severity of CAD without providing prognostic significance.
- Further clinical trials are needed to determine the appropriate strategy for managing CAD in severe AS.