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1 Ottobre
2022

TRATTAMENTO DELLA STENOSI VALVOLARE AORTICA

ANGIOPLASTICA CORONARICA IN PAZIENTI SOTTOPOSTI A TAVI: QUANDO EFFETTUARLA

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STS-ACC TVT Registry of Transcatheter Aortic Valve Replacement

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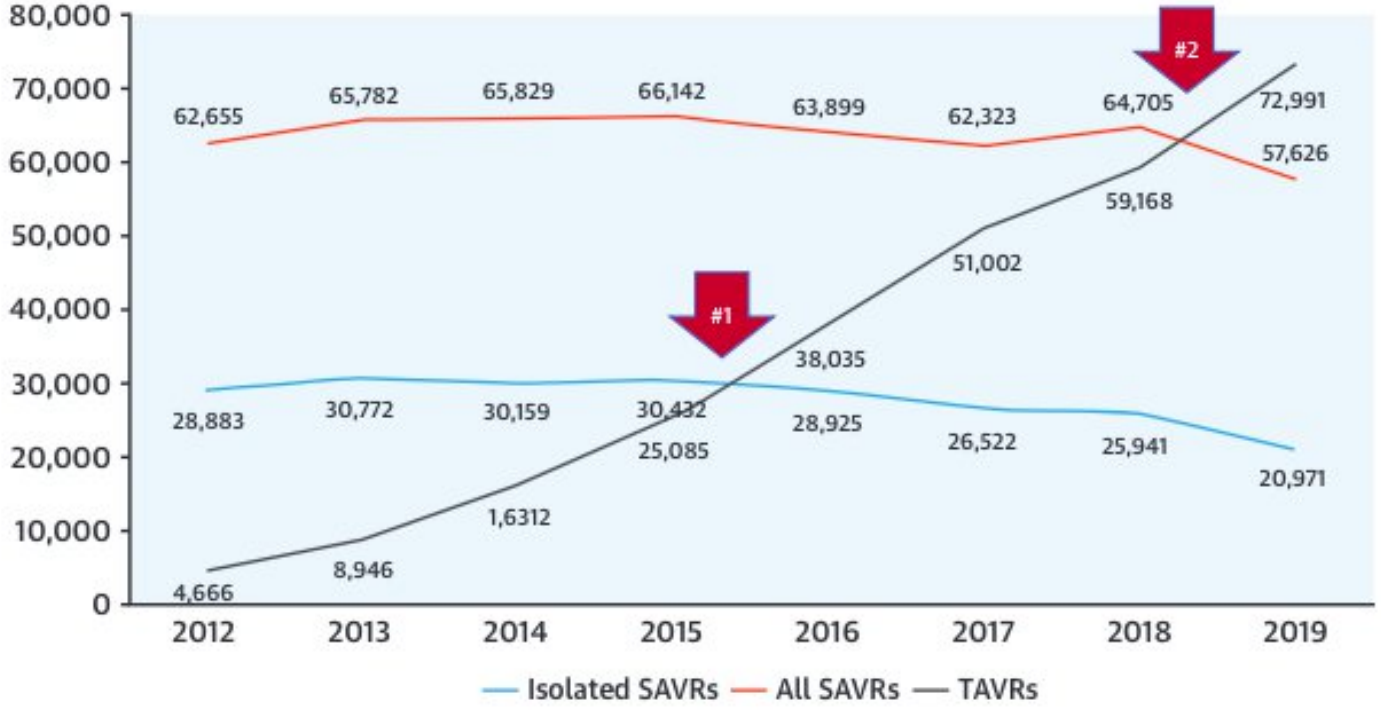
ABSTRACT

The STS-ACC TVT Registry (Society of Thoracic Surgeons–American College of Cardiology Transcatheter Valve Therapy is the first presentation on 8,395 low-risk patients treated in 2019. In 2019, for the entire cohort, femoral access increased to 95.3%, hospital stay was 2 days, and 90.3% were discharged home. Since 2011, the 30-day mortality rate has decreased (7.2% to 2.5%), stroke has started to decrease (2.75% to 2.3%), but pacemaker need is unchanged (10.9% to 10.8%). Alive with acceptable patient-reported outcomes is achieved in 8 of 10 patients at 1 year. The Registry is a national resource to improve care and analyze TAVR's evolution. Real-world outcomes, site performance, and the impact of coronavirus disease 2019 will be subsequently studied. (STS/ACC Transcatheter Valve Therapy Registry [TVT Registry]; NCT01737528) (J Am Coll Cardiol 2020;76:2492-516) © 2020 by The Society of Thoracic Surgeons and the American College of Cardiology Foundation.

Carroll, J.D. et al. J Am Coll Cardiol. 2020;76(21):2492-516



Carroll, J.D. et al. J Am Coll Cardiol. 2020;76(21):2492–516.

PARTNER 3

- RCT 1:1
- vs. Surgery
- N = 1000 pts

Low Risk

The NEW ENGLAND JOURNAL of MEDICINE

OCTOBER 21, 2010

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*

The NEW ENGLAND JOURNAL of MEDICINE

APRIL 28, 2016

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*

The NEW ENGLAND JOURNAL of MEDICINE

JUNE 9, 2011

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

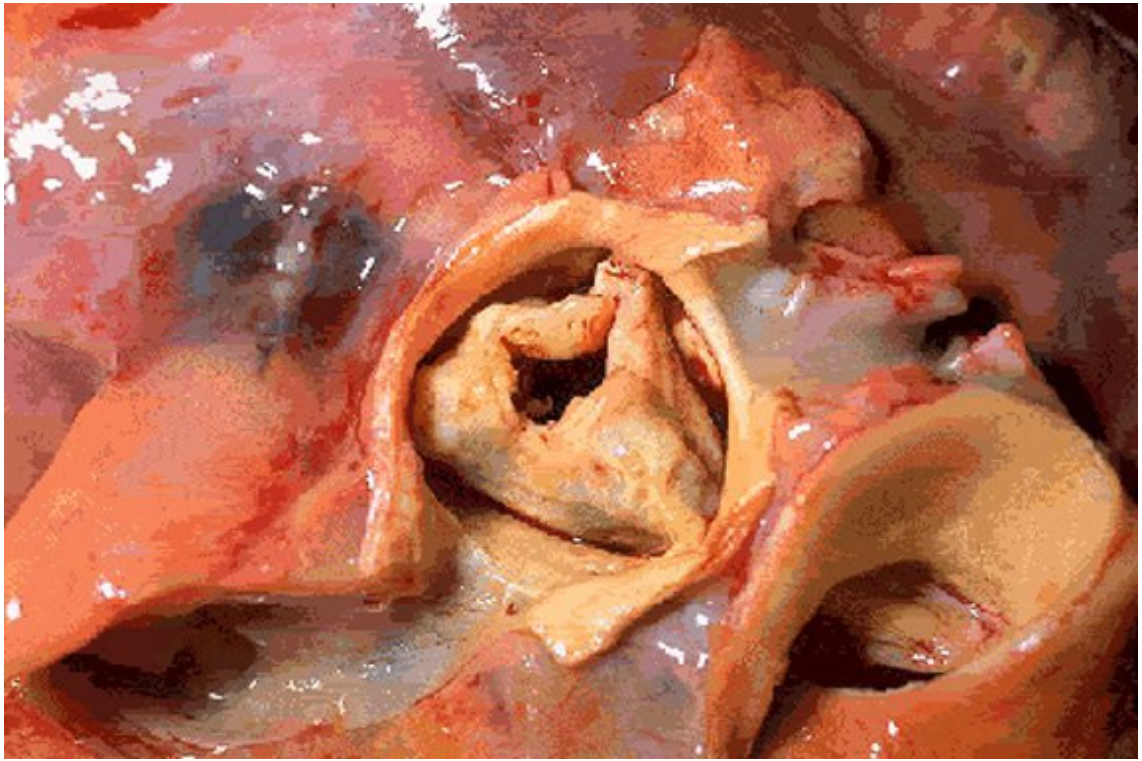
Craig R. Smith, M.D., Martin B. Leon, M.D., Michael J. Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., Mathew Williams, M.D., Todd Dewey, M.D., Samir Kapadia, M.D., Vasilis 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*

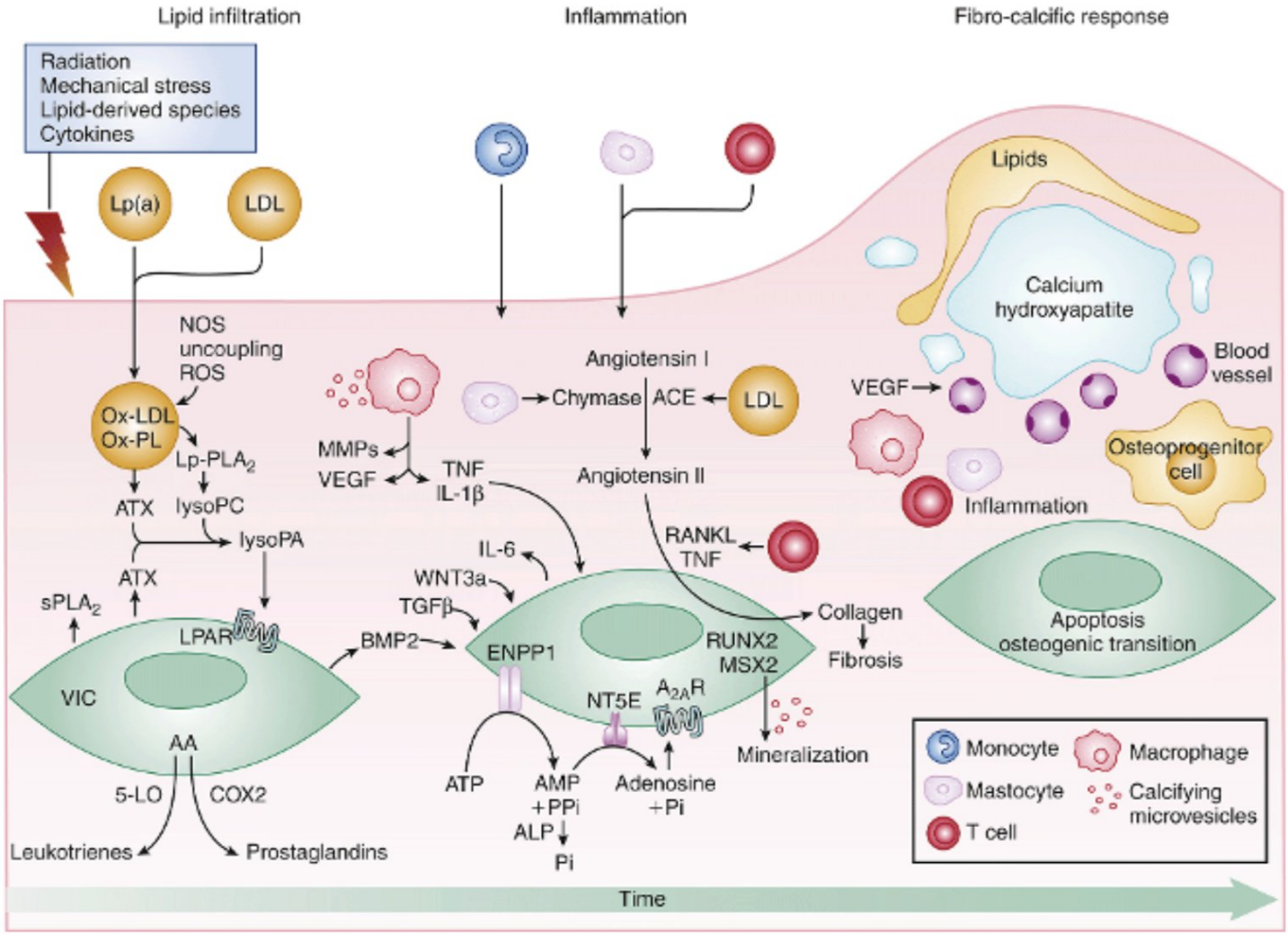
Aortic stenosis and coronary artery disease (CAD) frequently co-exist, as they share a common pathophysiology and risk factors.

Due to lack of randomised controlled trials (RCTs) and exclusion of significant CAD in transcatheter aortic valve replacement (TAVR) trials, the optimal method of revascularisation of CAD in patients undergoing TAVR remains unknown.

Coronary disease in TAVR patients is common: 40-80% of TAVR patients; 3.5-5.7% post TAVI PCI rates (likely to increase as TAVR expands to lower risk patients with greater life expectancy).

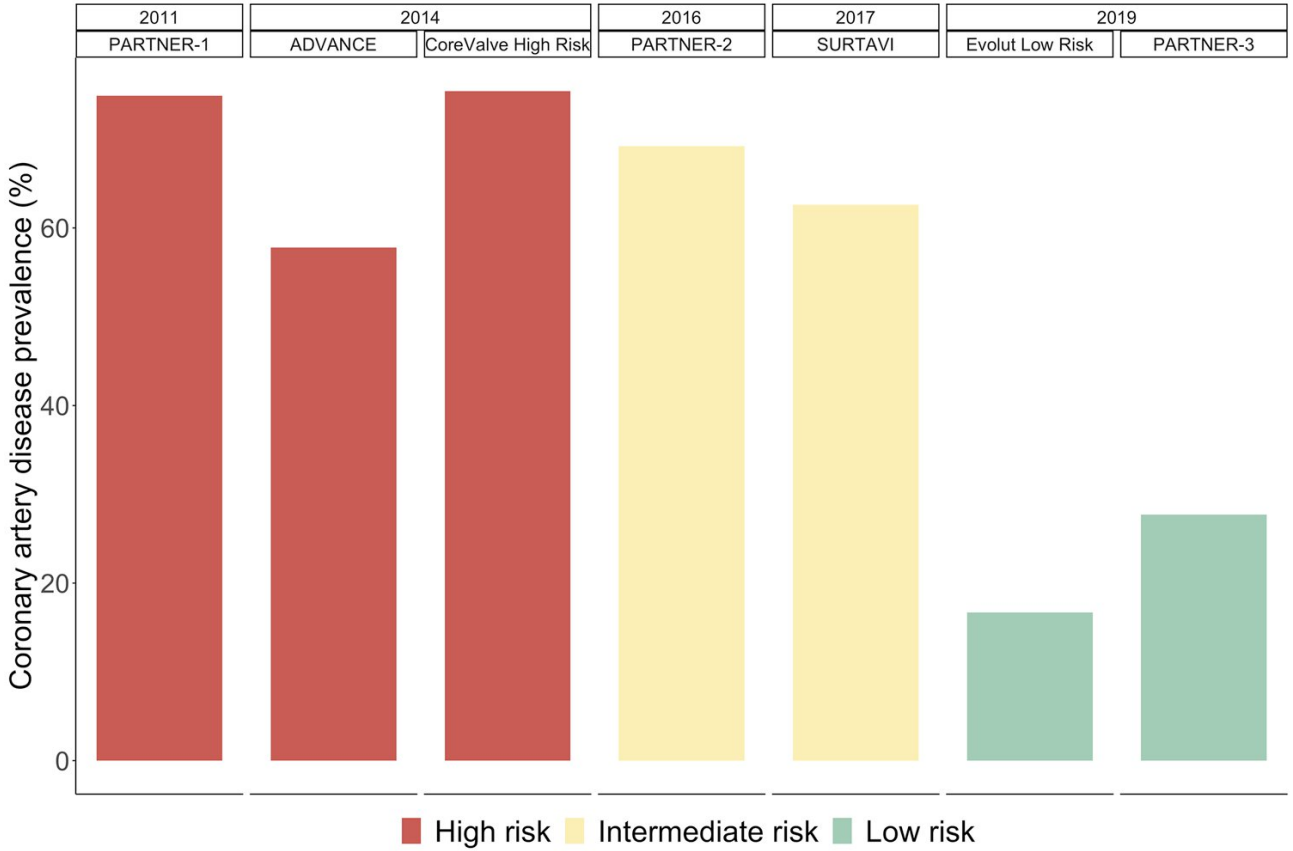
Katta N et al Heart International. 2020;14(1):24-8 DOI: https://doi.org/10.17925/HI.2020.14.1.24




Lipid infiltration
Inflammation
Fibro-calcific response
Radiation
Mechanical stress
Lipid-derived species
Cytokines
Lp(a)
LDL
NOS uncoupling ROS
Ox-LDL
Ox-PL
Lp-PLA2
ATX
lysoPC
lysoPA
ATX
sPLA2
LPAR
VIC
AA
5-LO
COX2
Leukotrienes
Prostaglandins
BMP2
MMPs
VEGF
TNF
IL-1β
Angiotensin I
Chymase
ACE
LDL
Angiotensin II
RANKL
TNF
IL-6
WNT3a
TGFβ
ENPP1
NT5E
A2AR
ATP
AMP +PPi
ALP
Pi
Adenosine +Pi
RUNX2
MSX2
Collagen
Fibrosis
Mineralization
Lipids
Calcium hydroxyapatite
VEGF
Blood vessel
Osteoprogenitor cell
Inflammation
Apoptosis osteogenic transition
Monocyte
Macrophage
Mastocyte
Calcifying microvesicles
T cell
Time

Clinical Impact of CAD in TAVR

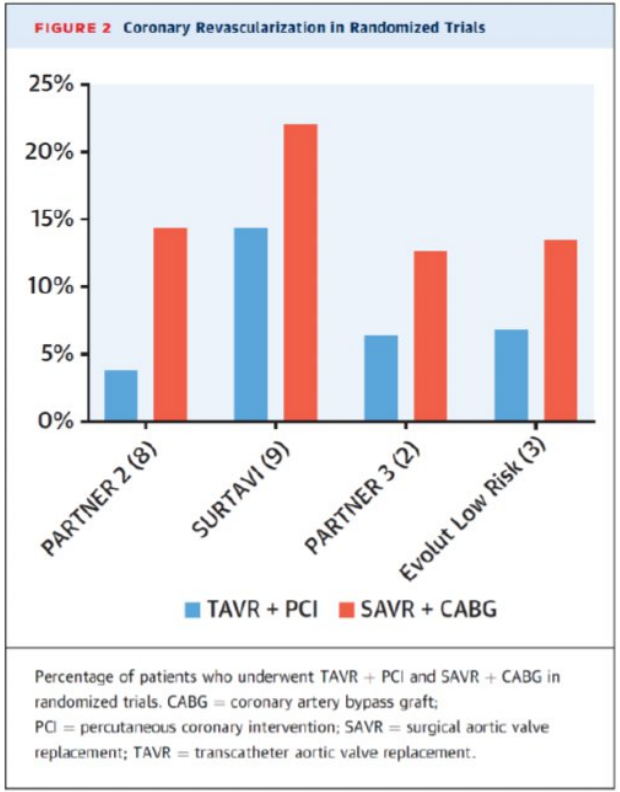
Prevalence of coronary artery disease in TAVR candidates reported in the main studies



Keller et al Current Cardiology Reports (2022) 24:1011–1020

Coronary Revascularization in RCTs…

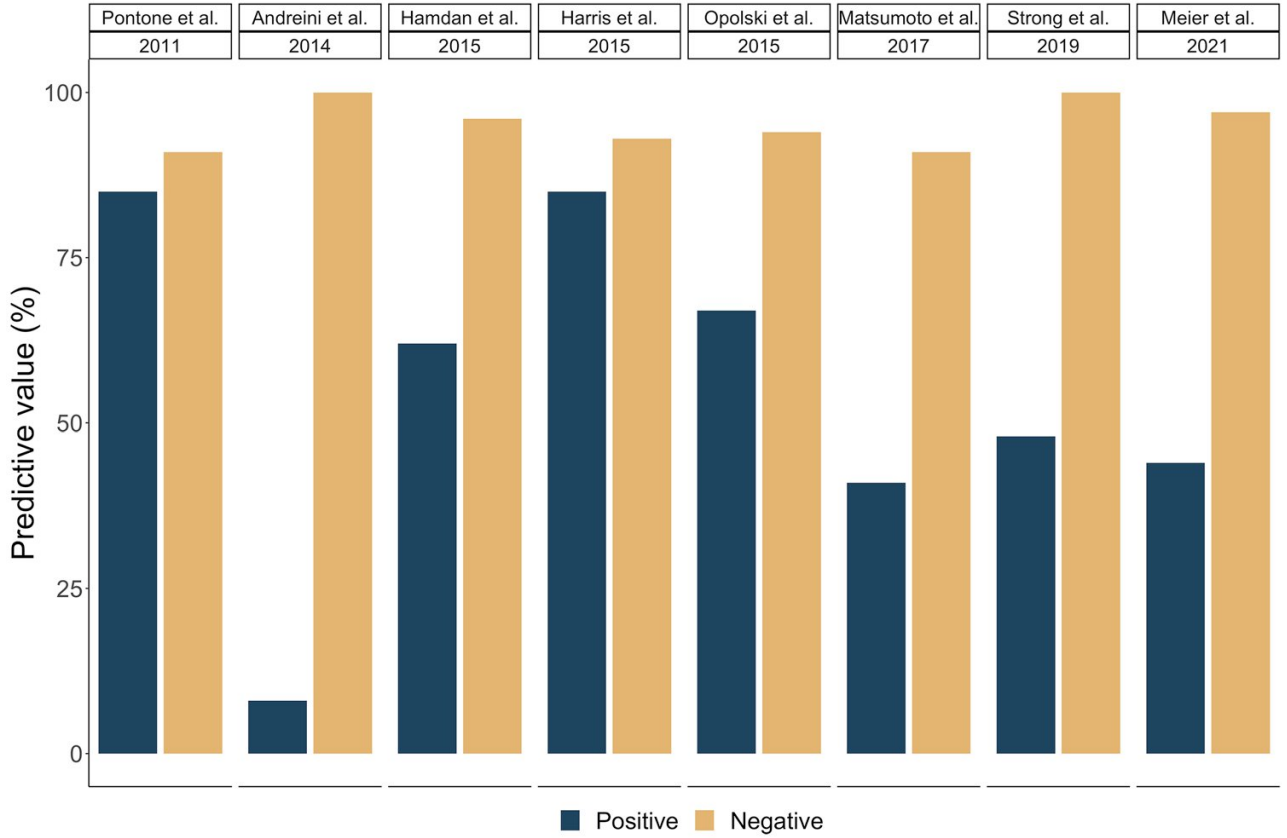
- 12% (4 - 22%) with concomitant revascularization
- TAVR + PCI (n = 32) vs SAVR + CABG (n = 58) in PARTNER 3
- SS > 22 (PARTNER 3) or 32 were excluded from RCTs



Farouxet al. JACC. July 2019

Assessment of CAD

Assessment of CAD: Accuracy of computed tomography angiography for detection of significant coronary artery disease in the TAVR work-up



Keller et al Current Cardiology Reports (2022) 24:1011–1020

Assessing and managing CAD in TAVR recipients: ongoing and future studies in the field

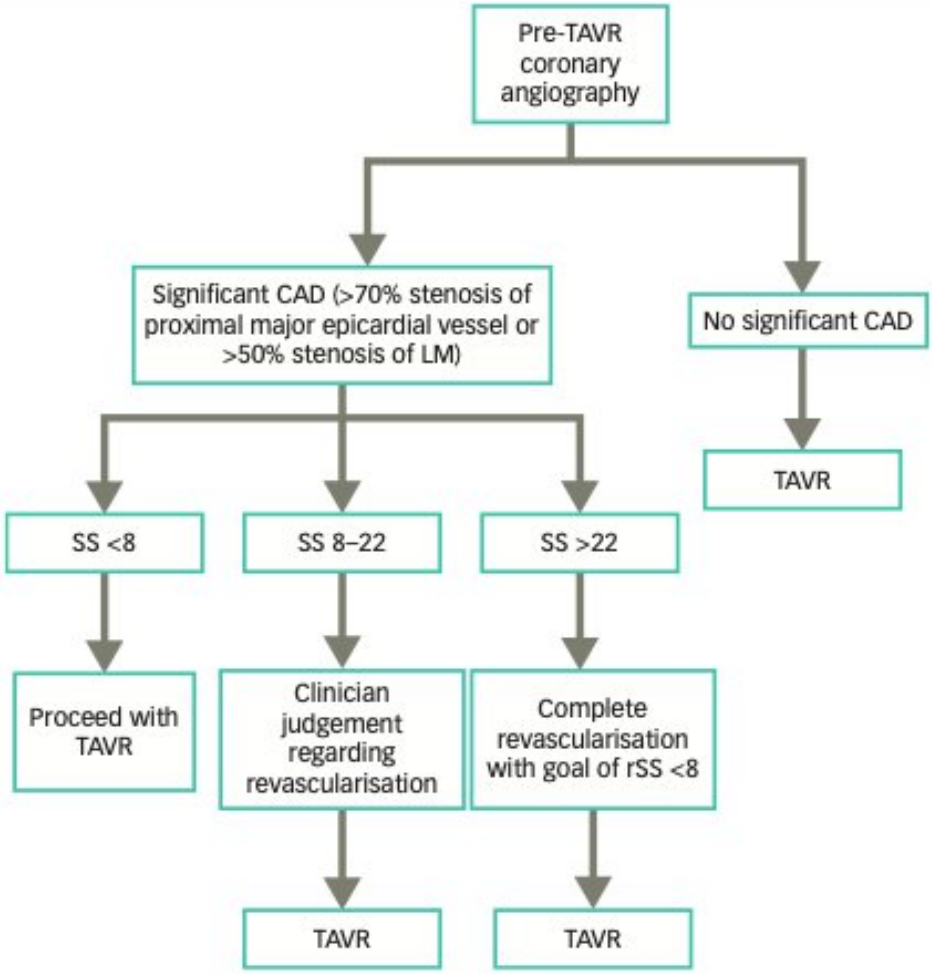
Study	Study design	n	Intervention	Primary endpoint
TCW NCT03424941	Randomized open-label non-inferiority trial	328	FFR-guided PCI + TAVR versus CABG + SAVR	Composite of all-cause mortality, myocardial infarction, disabling stroke, unscheduled clinically driven target vessel revascularization, valve reintervention, and life-threatening or disabling bleeding at 1 year
FAITAVI NCT03360591	Randomized open-label trial	320	Physiologically-guided strategy (PCI of lesions with FFR ≤ 0.80) versus 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 year
TAVI PCI NCT04310046	Randomized open-label trial	986	PCI in any suitable lesion (iwFR ≤ 0.8 or > 90% diameter stenosis in a coronary artery ≥ 2.5 mm) within 1-45d before TAVR versus within 1-45d after TAVR	All-cause death, non-fatal myocardial infarction, ischemia-driven revascularization, rehospitalization (valve- or procedure-related including heart failure), life-threatening/ disabling or major bleeding at 1 year
NOTION-3 NCT03058627	Randomized open-label trial	452	TAVR only versus TAVR + FFR-guided complete revascularization	All-cause mortality, myocardial infarction or urgent revascularization at 1 year

Keller et al Current Cardiology Reports (2022) 24:1011–1020

A potential limitation of FFR in this context relates to the potential alteration of coronary flow reserve as a consequence of the left ventricular hypertrophy commonly seen in severe aortic stenosis, which may result in an underestimation of the severity of coronary stenosis.

In contrast, iFR (assessing pressure ratio during the wave-free period of diastole) seems to be less influenced by the stenotic aortic valve and moreover does not require the administration of a vasodilator.

Keller et al Current Cardiology Reports (2022) 24:1011–1020



Katta N et al Heart International. 2020;14(1):24-8 DOI: https://doi.org/10.17925/HI.2020.14.1.24

- **Conclusion**
- In summary, in patients with CAD undergoing TAVR, the SYNTAX score can be a useful tool in deciding which patients may benefit from PCI prior to TAVR. In patients with high SYNTAX score (>22), we recommend performing PCI before TAVR to improve post-TAVR outcomes. In those with low SYNTAX score (<8), no additional coronary intervention is necessary and operators can proceed directly with TAVR. However, in those with intermediate SYNTAX score (8–22), the decision to perform PCI should be individualised based on the clinical risk factors in consultation with the heart team. Further large-scale RCTs are required to provide definitive answers regarding management of these complex groups of patients.

Katta N et al Heart International. 2020;14(1):24-8 DOI: https://doi.org/10.17925/HI.2020.14.1.24

Coronary revascularization of severe coronary lesions located in the proximal-mid segment of the coronary vessels remains common practice in most TAVR centers.

Recommendations for management of patients with CAD in VHD (ESC 2021)

Recommendations	Class	Level
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
PCI should be considered in patients with a primary indication to undergo transcatheter mitral valve intervention and coronary artery diameter stenosis >70% in proximal segments.	IIa	C

The low level of evidence of these recommendations reflects the uncertainties regarding the clinical impact of coronary revascularization in TAVR recipients with concomitant CAD

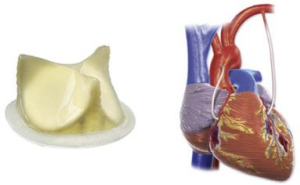
Revascularization in TAVR

CENTRAL ILLUSTRATION: Study Flowchart and Main Findings

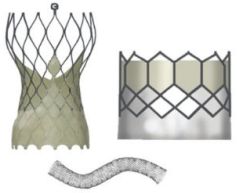
800 patients with severe aortic stenosis and complex coronary artery disease (SYNTAX score >22 or unprotected left main disease)

598 (74.8%) SAVR + CABG

202 (25.2%) Transfemoral TAVR + PCI



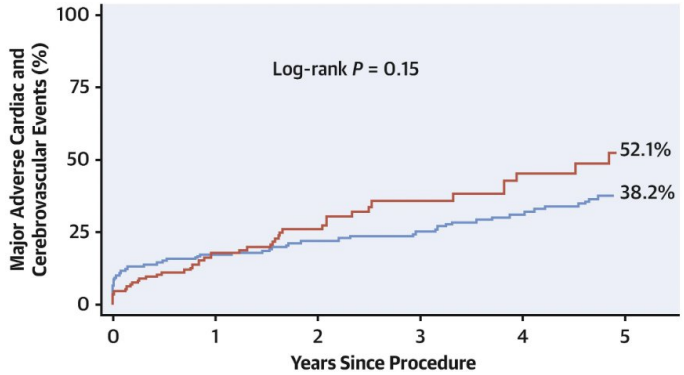
1:1 Propensity-matching



156 patients SAVR + CABG

156 patients TAVR + PCI

Primary endpoint: All-cause death, myocardial infarction, stroke, or new coronary revascularization



No. at risk:

SAVR + CABG	156	123	105	91	79	64
TAVR + PCI	156	93	58	30	22	11

Alperi, A. et al. J Am Coll Cardiol Intv. 2021;14(22):2490-2499.

ACTIVATION (PercutAneous Coronary inTervention prIor to transcatheter aortic VAlve implantaTION): A Randomized Clinical Trial

Objectives: This study sought to determine if percutaneous coronary intervention (PCI) prior to transcatheter aortic valve replacement (TAVR) in patients with significant coronary artery disease would produce noninferior clinical results when compared with no PCI (control arm).

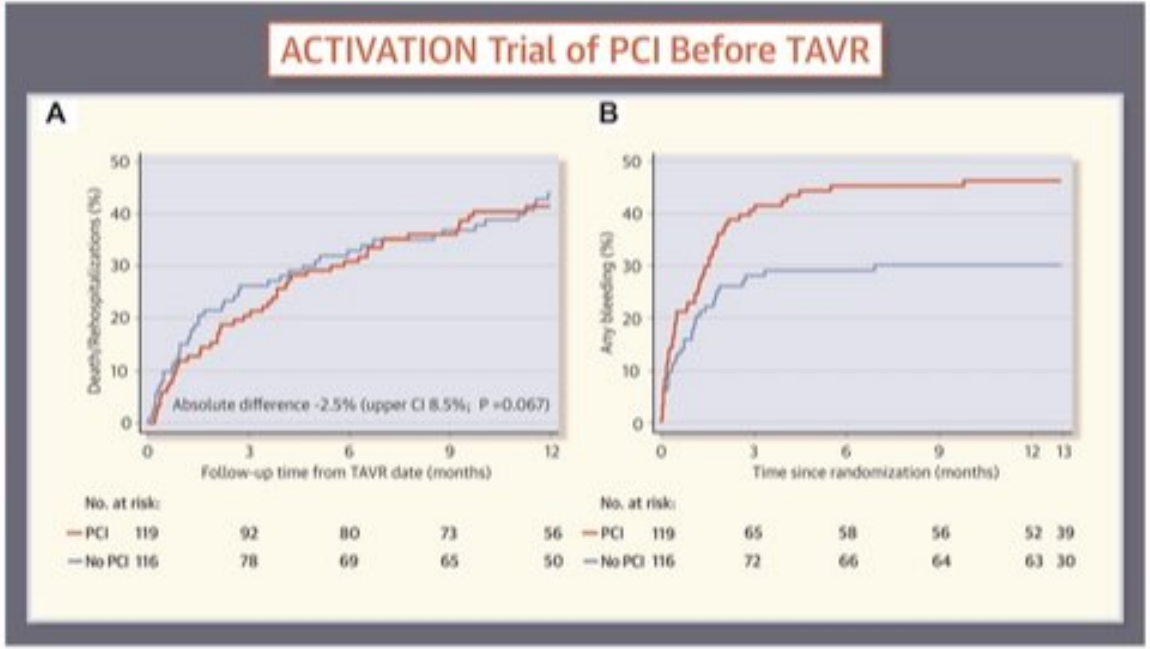
Background: PCI in patients undergoing TAVR is not without risk, and there are no randomized data to inform clinical practice.

Methods: Patients with severe symptomatic aortic stenosis and significant coronary artery disease with Canadian Cardiovascular Society class ≤2 angina were randomly assigned to receive PCI or no PCI prior to TAVR. The primary endpoint was a composite of all-cause death or rehospitalization at 1 year. Noninferiority testing (prespecified margin of 7.5%) was performed in the intention-to-treat population.

Results: At 17 centers, 235 patients underwent randomization. At 1 year, the primary composite endpoint occurred in 48 (41.5%) of the PCI arm and 47 (44.0%) of the no-PCI arm. The requirement for noninferiority was not met (difference; -2.5%; 1-sided upper 95% confidence limit;

Conclusions: Observed rates of death and rehospitalization at 1 year were similar between PCI and no PCI prior to TAVR; however, the noninferiority margin was not met, and PCI resulted in a higher incidence of bleeding. (Assessing the Effects of Stenting in Significant Coronary Artery Disease Prior to Transcatheter Aortic Valve Implantation; ISRCTN75836930).

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.

The results of the trial are widely interpreted as evidence that pre-TAVR PCI in patients > 80 years and stable coronary artery disease may not significantly improve the outcome but still comes along with additional risks.

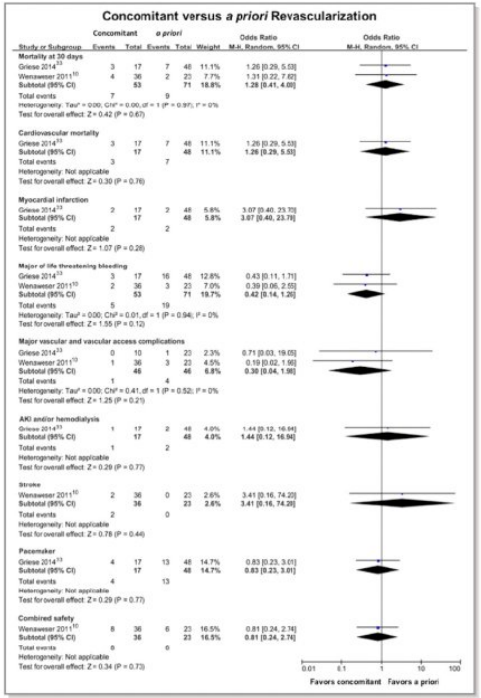
However, as the patient population eligible for TAVR changed since the start of the trial in 2011, the transferability of the trial results to younger and lower-risk patients has yet to be determined.

Furthermore, it will be of great interest to determine whether a complete revascularization-strategy guided by FFR may alter the outcome of PCI pre-TAVR. This question is currently addressed by the ongoing NOTION-3 trial.

Optimal Timing of PCI

PCI before, during or after?

Before vs Same setting



Same setting

Safe and no signal for harm

- Wenaweser et al. 2011
- Conradi et al. 2011
- Pasic et al. 2012
- Griese et al. 2014
- Penkalla et al. 2015
- Barbanti et al. 2017

Kotroniaset al, JAHA 2017

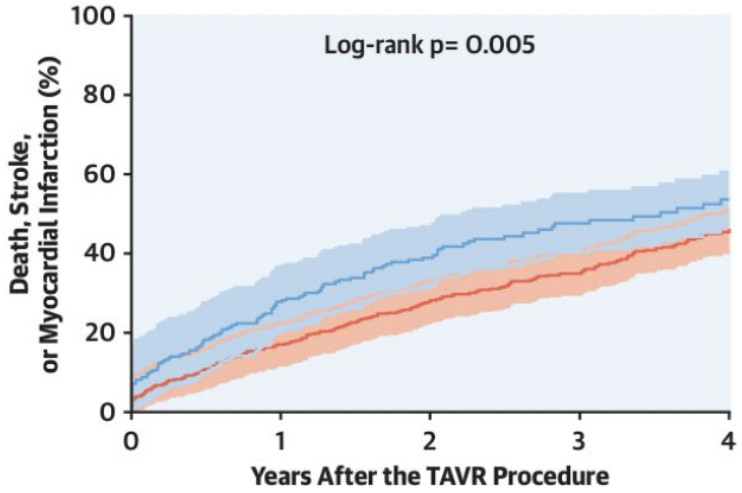
Percutaneous Coronary Intervention in the Workup Pre-Transcatheter Aortic Valve Replacement

Frequent complex coronary lesion (B2/C type, calcified, ostial location)

High procedural success rate (97.3%)

Low rate of target lesion failure:
- Stent thrombosis: 0.4%
- In-stent restenosis: 2.3%

Incomplete revascularization pre-TAVR determined an increased risk



No. at risk:					
Incomplete Revascularization	308	164	109	61	42
Complete Revascularization	889	560	342	225	147

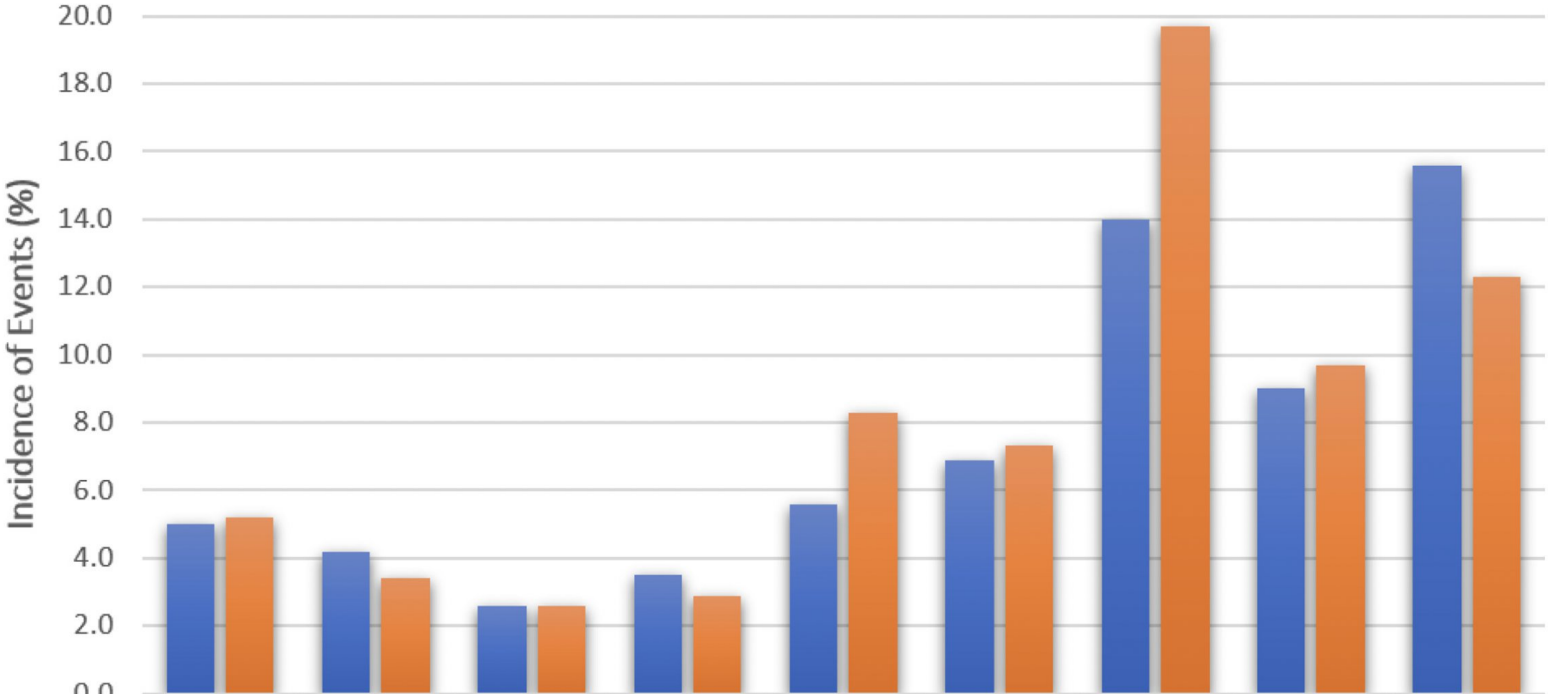
Faroux, L. et al. J Am Coll Cardiol Intv. 2020;■(■):■-■.

Current Problems in Cardiology
Volume 47, Issue 11, November 2022, 101339

Clinical Outcomes of Revascularization with Percutaneous Coronary Intervention Prior to Transcatheter Aortic Valve Replacement: A Comprehensive Meta-Analysis

Ahmed M. Altibi [a, #], Fares Ghanem [b, #], Faris Hammad [c], Jeentendra Patel [b], Howard K. Song [a], Harsh Golwala [a], Firas E. Zahr [a], Hind Rahmouni [a]

Pooled Event Rates (%) at 30-Day Following TAVR



	All-cause Mortality	CV Mortality	Stroke	MI	AKI	LTB	Any Bleed	MVC	PPM
No PCI	5.0	4.2	2.6	3.5	5.6	6.9	14.0	9.0	15.6
PCI	5.2	3.4	2.6	2.9	8.3	7.3	19.7	9.7	12.3

Altibi et al Curr Probl Cardiol 2022 Nov;47(11):101339.

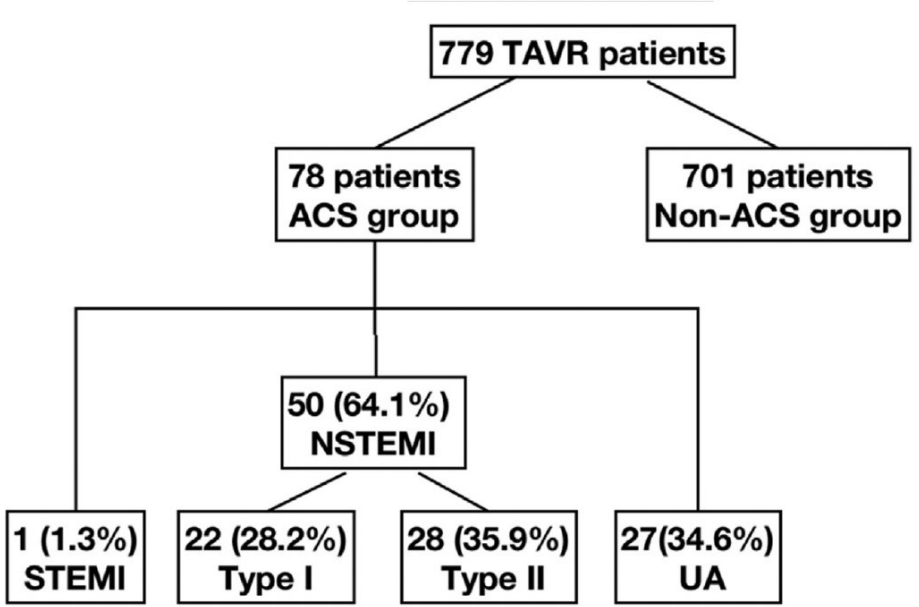
PCI before TAVR	PCI and TAVR simultaneously	PCI after TAVR
Pros	**Pros**	**Pros**
• Unhindered coronary access • Smaller risk for contrast-induced nephropathy (minimized contrast load) Reduced ischemic burden pre-TAVR	• Single puncture • Reduced hospitalization length	• Reduced bleeding risk (no DAPT) pre-TAVR • Better accuracy of hemodynamic functional assessment • Lower risk for contrast-induced nephropathy (Contrast media)
Cons	**Cons**	**Cons**
• Additional vascular puncture • Increased bleeding risk (TAVR under DAPT) • Possible hemodynamic deterioration during PCI	• Increased risk for contrast-induced nephropathy (increased contrast load) • Increased procedure length (patient discomfort)	• Significant ischemic burden during TAVR • Potential difficulties regarding coronary access

Keller et al Current Cardiology Reports (2022) 24:1011–1020

ACS after TAVR

ACS after TAVR

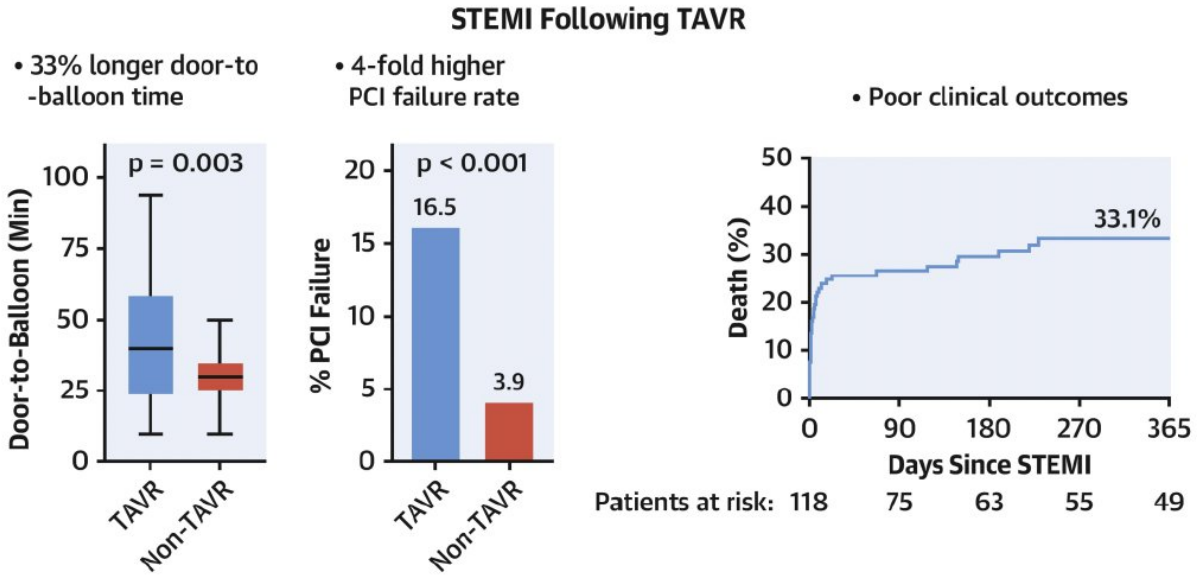
- 10% had an ACS after TAVR
- Median follow-up of 25 months
- 68% of patients had a prior Hx of CAD



Vilaltaet al, JACC Int 2018

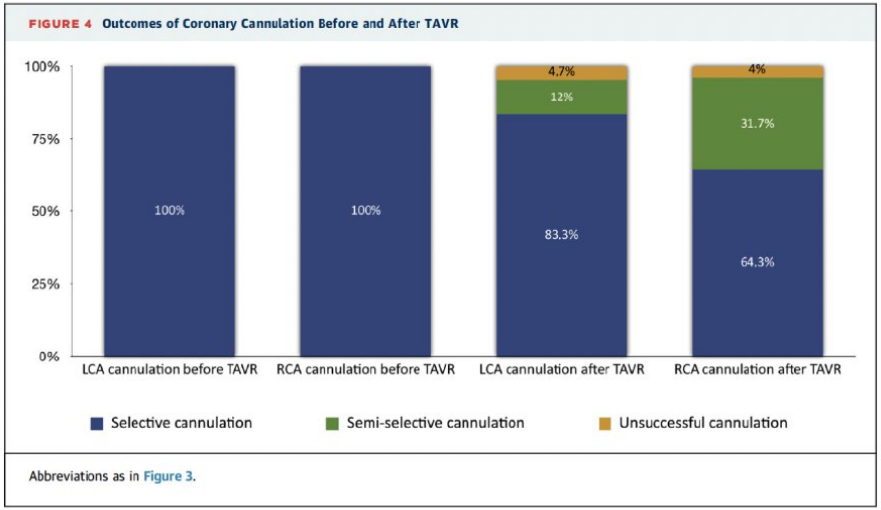
ST Elevation after TAVR

CENTRAL ILLUSTRATION: ST-Segment Elevation Myocardial Infarction Following Transcatheter Aortic Valve Replacement

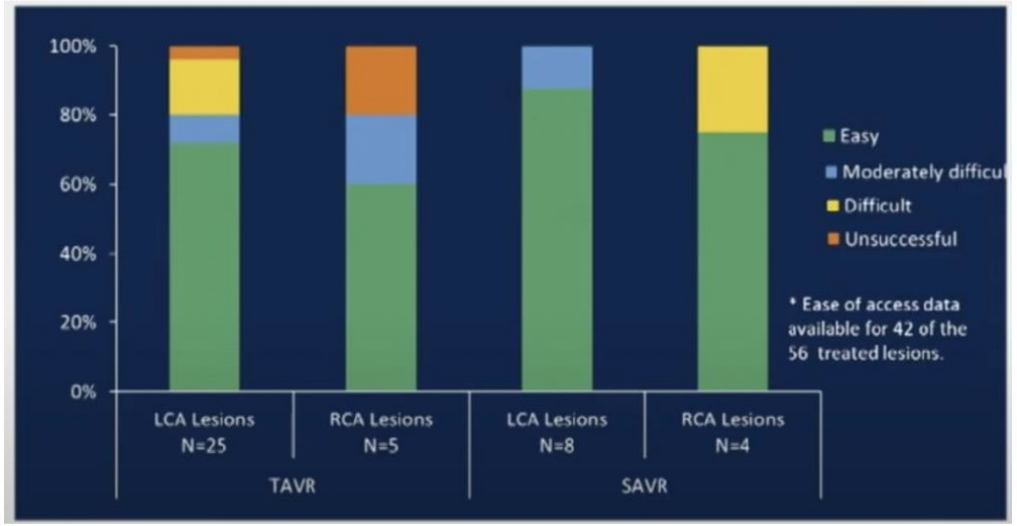


Faroux, L. et al. J Am Coll Cardiol. 2021;77(17):2187-99.

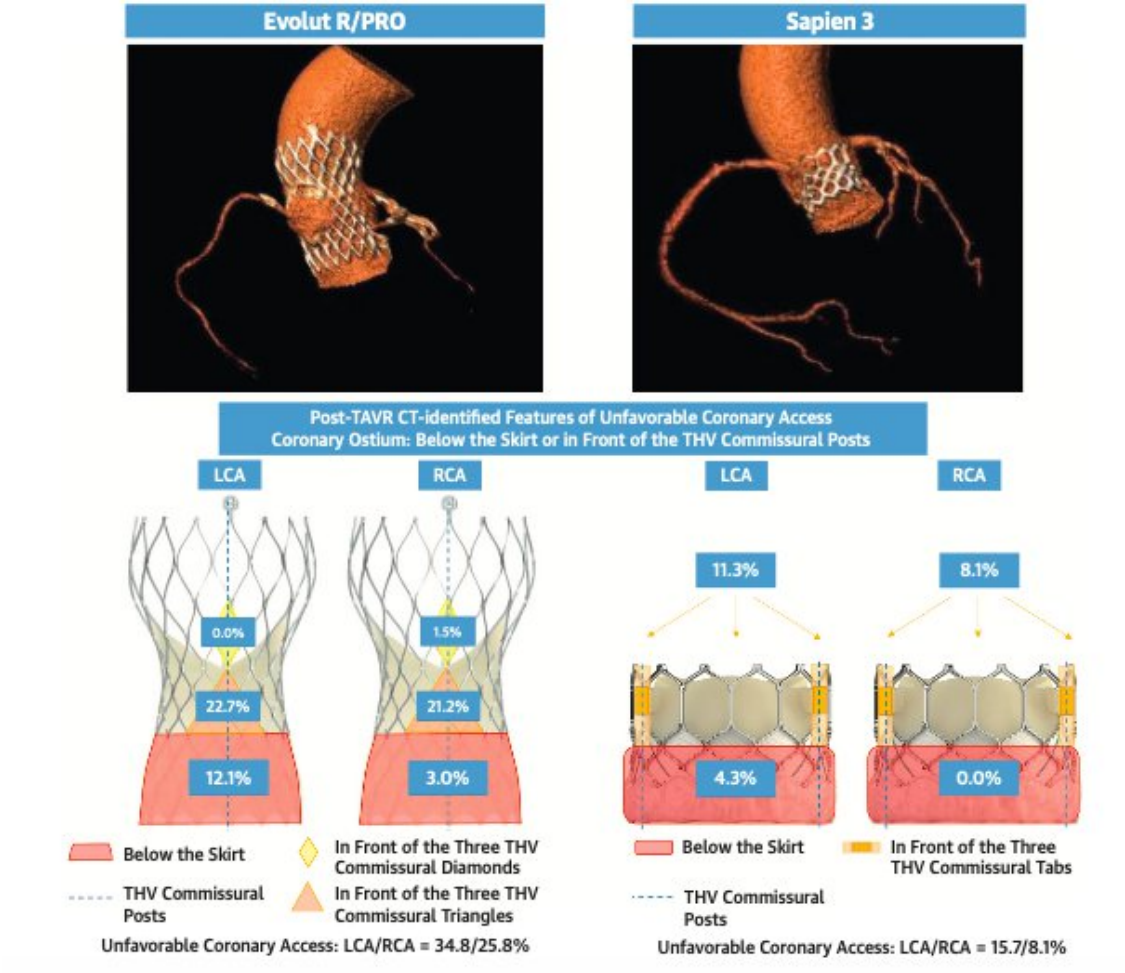
Coronary access after TAVR may be challenging



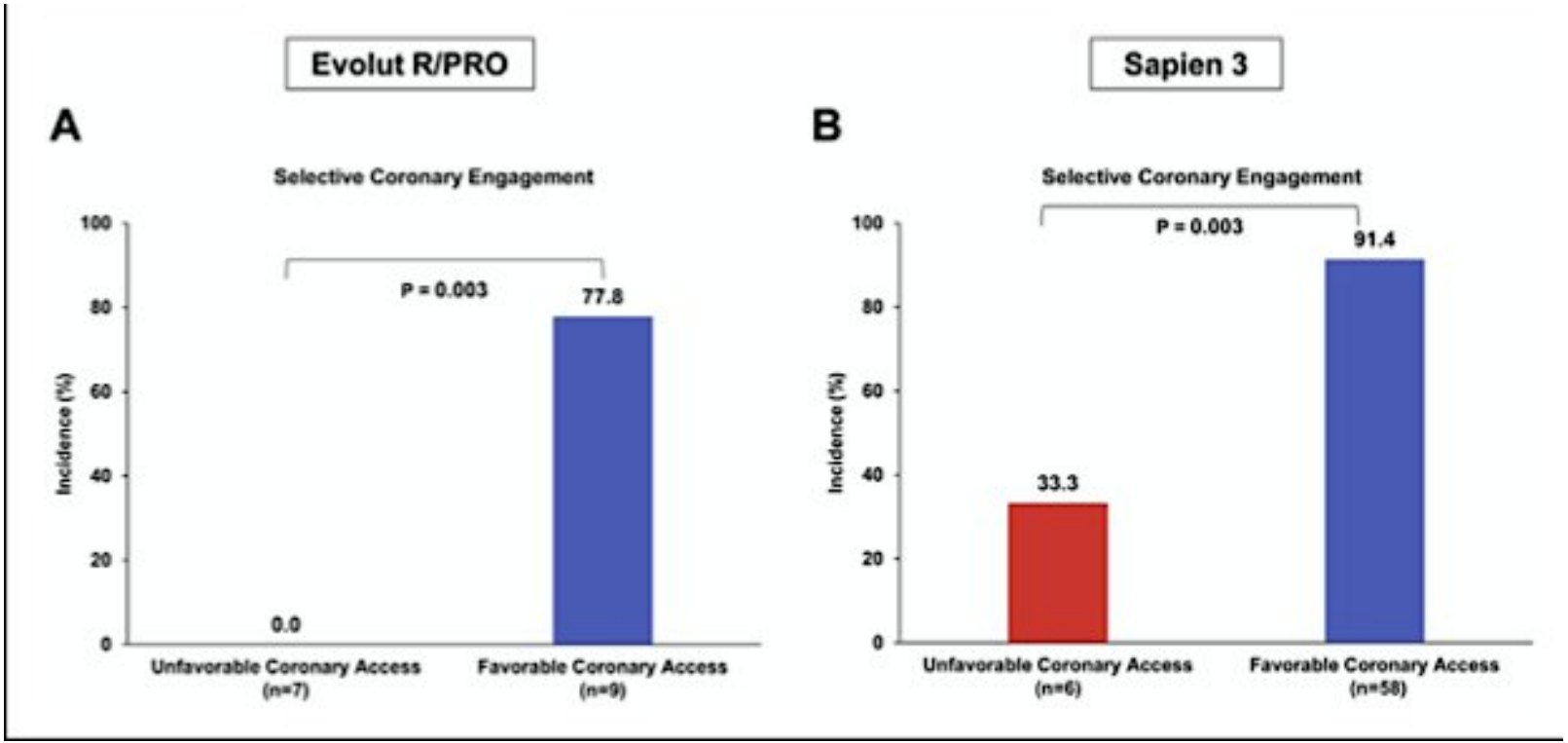
Barbanti et al



SURTAVI

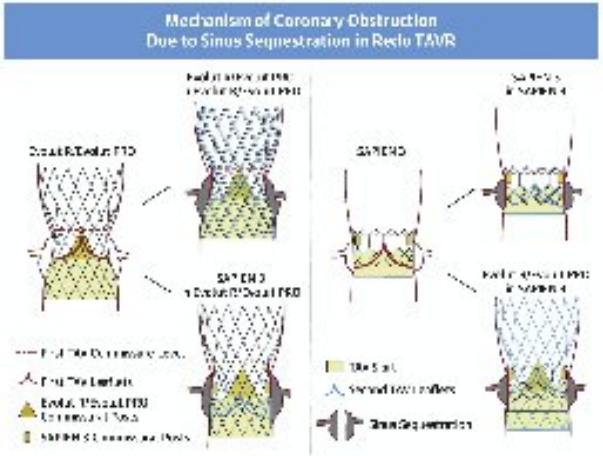


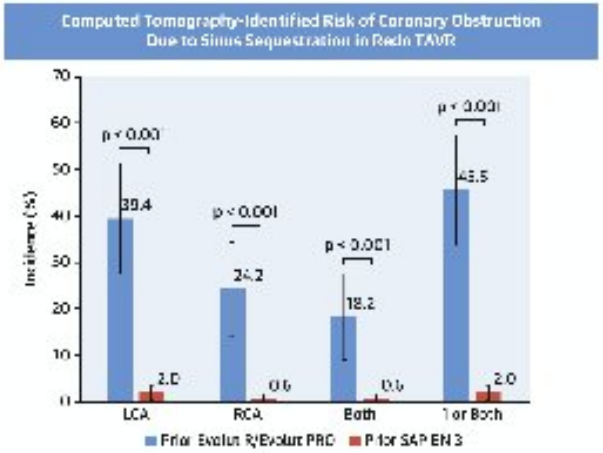
Ochiai T et al JACC: CARDIOVASCULAR INTERVENTIONS VOL. 13, N



Ochiai T elt al JACC: CARDIOVASCULAR INTERVENTIONS VOL. 13, N

CENTRAL ILLUSTRATION: CT-Identified Risk of Coronary Obstruction Due to Sinus Sequestration in Redo TAVR





Ochiai, T. et al. J Am Coll Cardiol Intv. 2020;13(22):2617–27.

COMPLETE TAVR

A Randomized, Comparative Effectiveness Study of Staged Complete Revascularization with PCI to Treat CAD vs Medical Management Alone in Patients with Symptomatic AV Stenosis undergoing Elective TAVR:

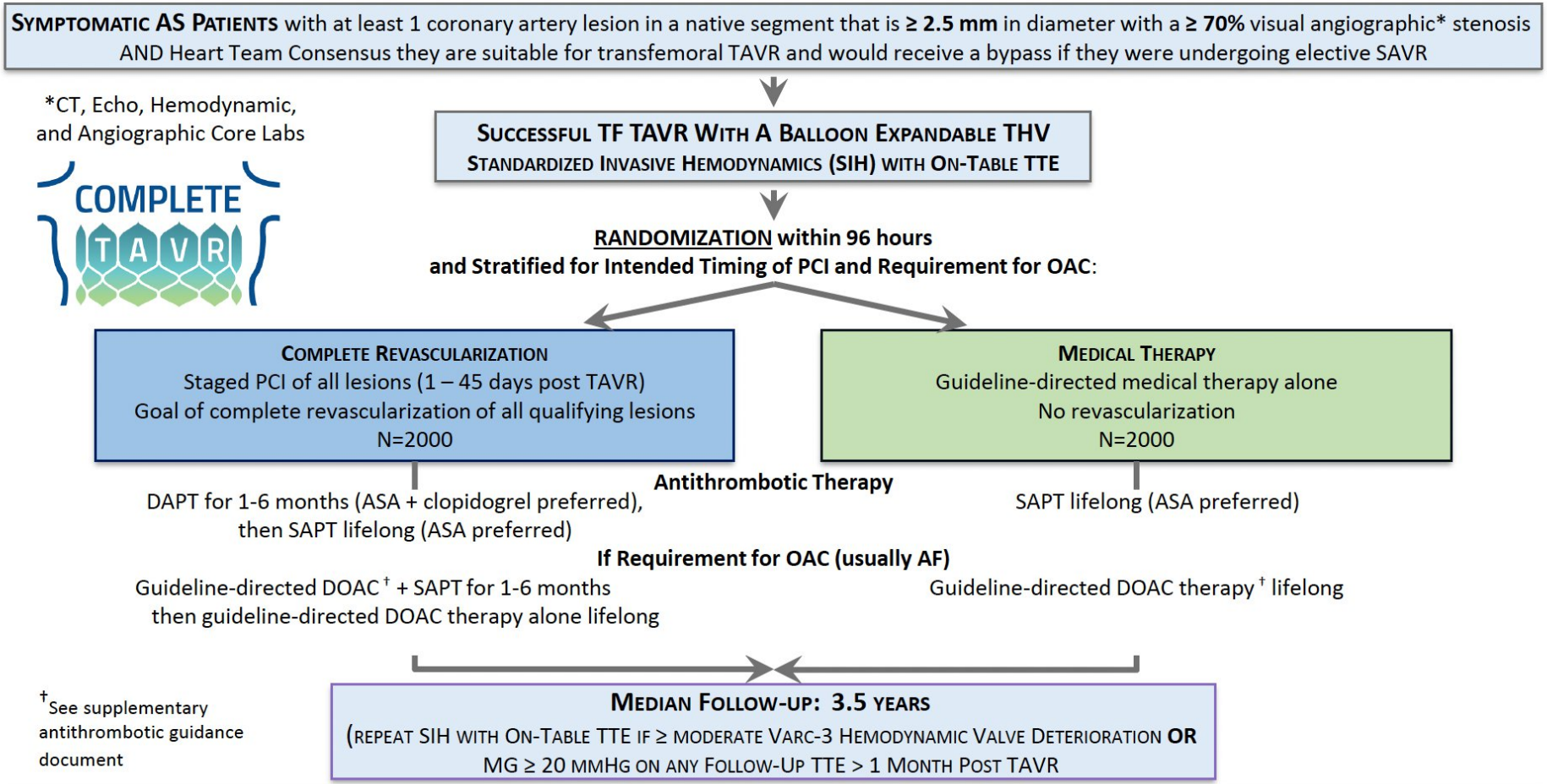
The COMPLETE TAVR Study

TVT June 8th, 2022 (In-person and Virtual)

CCI-CIC Centre for Cardiovascular Innovation
Centre d'Innovation Cardiovasculaire

COMPLETE TAVR

ClinicalTrials.gov Identifier NCT04634240


SYMPTOMATIC AS PATIENTS with at least 1 coronary artery lesion in a native segment that is ≥ 2.5 mm in diameter with a ≥ 70% visual angiographic* stenosis AND Heart Team Consensus they are suitable for transfemoral TAVR and would receive a bypass if they were undergoing elective SAVR
*CT, Echo, Hemodynamic, and Angiographic Core Labs
COMPLETE TAVR
SUCCESSFUL TF TAVR WITH A BALLOON EXPANDABLE THV
STANDARDIZED INVASIVE HEMODYNAMICS (SIH) WITH ON-TABLE TTE
RANDOMIZATION within 96 hours
and Stratified for Intended Timing of PCI and Requirement for OAC:
COMPLETE REVASCULARIZATION
Staged PCI of all lesions (1 – 45 days post TAVR)
Goal of complete revascularization of all qualifying lesions
N=2000
MEDICAL THERAPY
Guideline-directed medical therapy alone
No revascularization
N=2000
Antithrombotic Therapy
DAPT for 1-6 months (ASA + clopidogrel preferred), then SAPT lifelong (ASA preferred)
SAPT lifelong (ASA preferred)
If Requirement for OAC (usually AF)
Guideline-directed DOAC † + SAPT for 1-6 months then guideline-directed DOAC therapy alone lifelong
Guideline-directed DOAC therapy † lifelong
†See supplementary antithrombotic guidance document
MEDIAN FOLLOW-UP: 3.5 YEARS
(REPEAT SIH WITH ON-TABLE TTE IF ≥ MODERATE VARC-3 HEMODYNAMIC VALVE DETERIORATION OR MG ≥ 20 MMHG ON ANY FOLLOW-UP TTE > 1 MONTH POST TAVR
PRIMARY OUTCOME: Composite of CV Death, New MI, Ischemia-Driven Revascularization, or Hospitalization for Unstable Angina or for Heart Failure
KEY SECONDARY OUTCOMES: CV death or new MI, transaortic gradient post TAVR (echocardiographically-derived vs. direct invasive measurement)
SECONDARY OUTCOMES: Hemodynamic variables obtained with SIH and TTE, Each component of the primary outcome, Angina Status, All-cause Mortality, Stroke, Cost-effectiveness, QOL, Bleeding, Contrast Associated Acute Kidney Injury, Fluoroscopic Time/Contrast Utilization for Staged PCI

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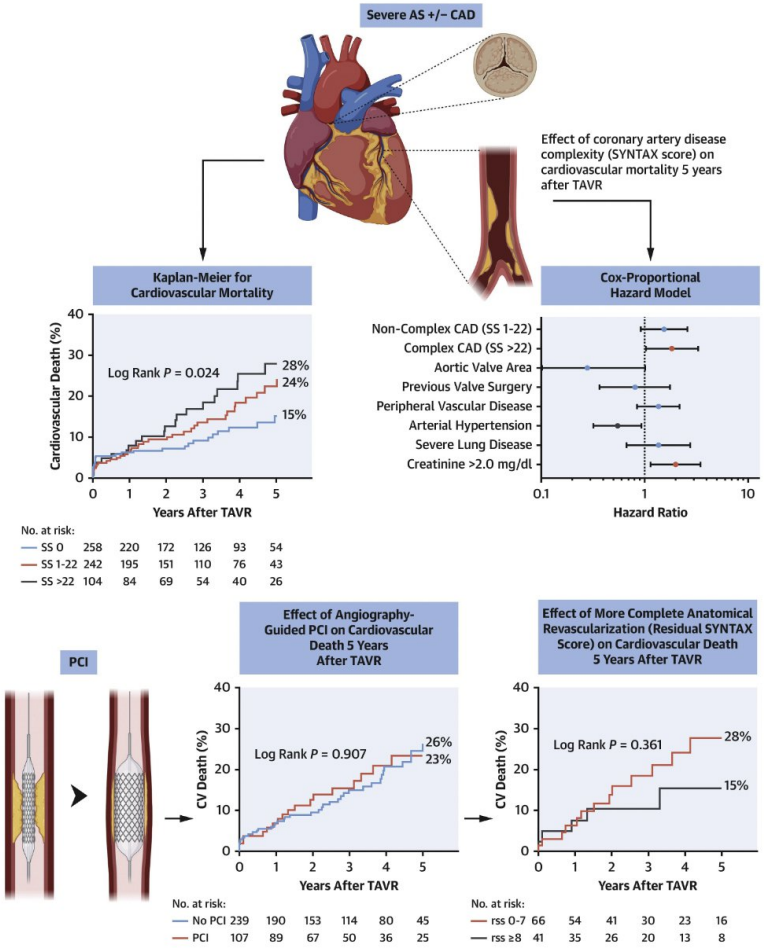
New Research Paper

Coronary

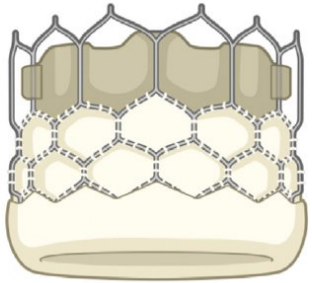
The Effect of Coronary Lesion Complexity and Preprocedural Revascularization on 5-Year Outcomes After TAVR

Lennert Minten MD [a, b], Pauline Wissels MD [a], Keir McCutcheon MD, PhD [a], Johan Bennett MD PhD [a, b], Tom Adriaenssens MD, PhD [a, b], Walter Desmet MD, PhD [a, b], Peter Sinnaeve MD PhD [a, b], Peter Verbrugghe MD, PhD [a, c], Steven Jacobs MD, PhD [a, c], Ipek Guler PhD [d], Christophe Dubois MD, PhD [a, b]

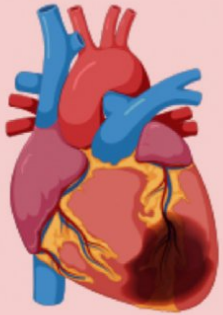
CENTRAL ILLUSTRATION: The Effect of CAD Complexity and Revascularization With PCI on Cardiovascular Mortality 5 Years After TAVR



Minten L, et al. J Am Coll Cardiol Intv. 2022;15(16):1611-1620.



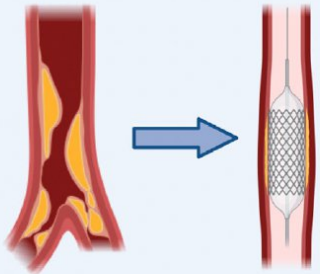
CAD ASSESSMENT



To be performed in all TAVR recipients for long-term CV risk stratification

- Anatomical complexity (SYNTAX score)
- Functional significance (iFR better than FFR)

PREVENTIVE PCI



To be considered in selected patients to reduce CV mortality

- Single-vessel, functionally significant CAD
- Patients with long expected survival
- Higher ischemic than bleeding risk
- Challenging coronary re-access (ViV, low coronary ostia, narrow STJ)

Stefanini and Gitto J A C C : C A R D I O V A S C U L A R I N T E R V E N T I ON S V OL . 1 5 , NO. 1 6 , 2 0 2 2

Conclusions

- Coronary artery disease is a common finding in patients with advanced degenerative aortic stenosis.
- The current practice in many centers to routinely perform an invasive coronary angiography as part of the TAVR workup got lately challenged by newer data showing a high diagnostic accuracy of CTA to exclude relevant coronary artery disease.
- As TAVR is increasingly considered a valid treatment option in younger patients with lower-risk and longer life expectancy, the handling of concomitant coronary lesions becomes more relevant.
- While the current ACC/AHA guidelines recommend PCI before TAVR, the European guidelines do not recommend a specific timing.
- In theory, the unhindered coronary access, the reduction of ischemic burden prior to TAVR, and the smaller amount of contrast media when administered in two sessions (staged procedures) indicate a possible benefit of the strategy to revascularize prior to TAVR.