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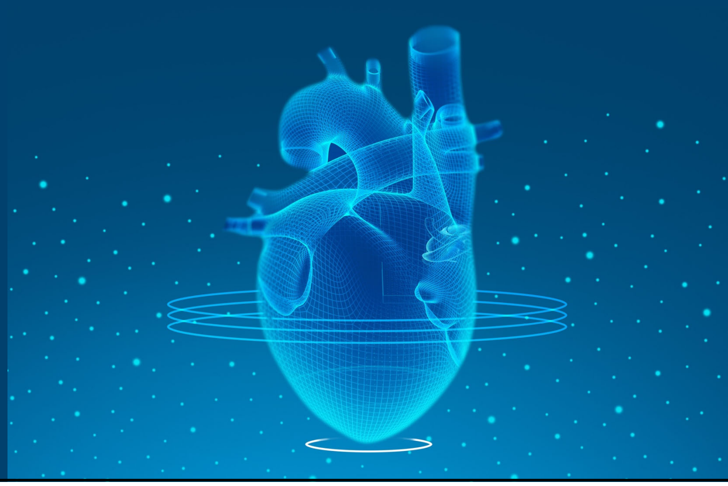
GRAND ROUNDS



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Tricuspid Valve Damage Associated with Implantation of Leadless Pacemakers.

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Disclosures

- None

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Background

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Approved RV Leadless Pacemakers

	Micra VR	Micra AV	AVEIR VR	RV.AVEIR DR
Manufacturer	Medtronic		Abbott	
Approval year	Apr.2016	Jan.2020	Mar.2022	Jun.2023
USA implanted devices since approval	71,898	68,885	8,504	N/A
Device				

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Pivotal Clinical Trials

Table 2. Major Complications in 725 Patients Who Underwent a Transcatheter Pacemaker Implantation Attempt.

Adverse Event	No. of Events Associated with Major Complication Criterion*						No. of Patients (%)†
	Death	Loss of Device Function	Hospitalization	Prolonged Hospitalization‡	System Revision	Total Events	
Embolism and thrombosis	0	0	1	1	0	2	2 (0.3)
Deep vein thrombosis	0	0	0	1	0	1	1 (0.1)
Pulmonary thromboembolism	0	0	1	0	0	1	1 (0.1)
Events at groin puncture site: atrioventricular fistula or pseudoaneurysm	0	0	2	3	0	5	5 (0.7)
Traumatic cardiac injury: cardiac perforation or effusion	0	0	3	9	0	11	11 (1.6)
Pacing issues: elevated thresholds	0	1	2	1	2	2	2 (0.3)
Other events	1	0	5	4	1	8	8 (1.7)
Acute myocardial infarction	0	0	0	1	0	1	1 (0.1)
Cardiac failure	0	0	3	2	0	3	3 (0.9)
Metabolic acidosis	1	0	0	0	0	1	1 (0.1)
Pacemaker syndrome	0	0	1	0	1	1	1 (0.2)
Presyncope	0	0	0	1	0	1	1 (0.1)
Syncope	0	0	1	0	0	1	1 (0.1)
Total	1	1	13	18	3	28	25 (4.0)

Micra VR; Reynolds et al. 2016

Event	Phase 1 Primary Cohort (n = 300)			Phase 2 Primary Cohort (n = 200)		
	No. of Events	No. of Patients	Event Rate, %	No. of Events	No. of Patients	Event Rate, %
Total	**22**	**20[1]**	**6.7%**	**9**	**8[1]**	**4.0%**
Cardiac perforation/tamponade/pericardial effusion	4	4	1.3%	3	3	1.5%[2]
Premature deployment with device migration	0	0	0.0%	2	2	1.0%[3]
Premature deployment without device migration	0	0	0.0%	1	1	0.5%[4]
Access site bleeding event	2	2	0.7%	1	1	0.5%
Pulmonary embolism	1	1	0.3%	1	1	0.5%
Deep vein thrombosis	0	0	0.0%	1	1	0.5%
Device dislodgement	5	5	1.7%	0	0	0.0%
Threshold elevation resulting in LP retrieval	4	4	1.3%	0	0	0.0%
Arteriovenous fistula	1	1	0.3%	0	0	0.0%
Pseudoaneurysm	1	1	0.3%	0	0	0.0%
Asystole during implant procedure	1	1	0.3%	0	0	0.0%
Ventricular tachycardia or ventricular fibrillation during implant procedure	1	1	0.3%	0	0	0.0%
Pericarditis	1	1	0.3%	0	0	0.0%
Orthostatic hypotension with weakness	1	1	0.3%	0	0	0.0%

AVEIR VR; Reddy et al. 2022

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Focus on Clinical Performance

Update on AVEIR™ VR Performance

The Aveir VR leadless pacemaker exhibits characteristics which are similar to both implantable pulse generators and cardiac leads. Device malfunction criteria are reported according to standard pacemaker laboratory-confirmed processes. In addition, Abbott has assessed the events reported in the United States according to the relevant hierarchical criteria listed in ISO 5841-2 (E) for cardiac leads. The tables below provide an overview of the product performance from Aveir VR approval to June 30, 2024.

DAY OF IMPLANT OBSERVATIONS (N = 8,504)

REPORTED COMPLICATION	QTY	RATE
Cardiac Perforation	37	0.44%
Dislodgement (Post Tether Mode)	37	0.44%
Failure to Capture	5	0.06%
Oversensing	1	0.02%
Failure to Sense	1	0.02%
Abnormal Impedance	3	0.04%

ACUTE OBSERVATIONS: OCCURRING WITHIN THE FIRST 30 DAYS POST-IMPLANT (N = 8,504)

REPORTED COMPLICATION	QTY	RATE
Cardiac Perforation	0	0%
Dislodgement	17	0.20%
Failure to Capture	10	0.12%
Oversensing	0	0%
Failure to Sense	1	0.02%
Abnormal Impedance	1	0.02%

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JOURNAL ARTICLE

Tricuspid valve complications during leadless pacemaker implantation FREE

R Hauser, S Casey, J Sengupta

EP Europace, Volume 24, Issue Supplement_1, May 2022, euac053.398, https://doi.org/10.1093/europace/euac053.398
Published: 19 May 2022

Results

From 2016-October 2021, 19 patients suffered a tricuspid valve adverse event, including damage to the leaflets, papillary muscle, or chordae tendineae (n=14; 74%); interference with valve closure (n=3; 16%); and 2 LPMs were irretrievably wedged in the tricuspid valve apparatus. Damaged valves included: 1) torn leaflet or chordal tissue found in the delivery system (n=6) after complicated or failed LPM recapture that necessitated removal without the LPM retracted into the delivery system; all patients developed tricuspid regurgitation, and one patient died. 2) valve damage by the delivery system either directly (n=6) or during LPM recapture (n=1) or removal by a snare (n=1); all patients had new or worsening tricuspid regurgitation; one patient died, 2 had valve repair, and one valve was replaced. In three patients the LPM interfered with valve closure; one patient had valve replacement, one underwent LPM removal, and one was treated medically. Of the 2 LPMs wedged in the tricuspid valve apparatus, one required surgical removal and one was abandoned.

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Aim and Methods

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Aim

- The aim of our study is to update the Micra experience regarding TV damage occurring during implantation of LPs
- Determine if AVEIR implantation may also be associated with TV injury during LP implantation.

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Methodology

A MAUDE Database Retrospective study

Patients who suffered procedure-related tricuspid valve damage/injury

Worldwide Centers, since April 2016 to March 2025

Major adverse clinical events; Death, Heart Failure, or Tricuspid valve intervention

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Results

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Results

- We found 45 patients who suffered from procedure-related TV injuries during LP implantation from centers worldwide.
- Median patient age was 81 (72,87) years and half of the patients were females (50%).
- Micra VR and AV (n=41; 91%), and AVEIR VR (n=4; 9%).
- Most events (n=31; 69%) occurred outside the US.

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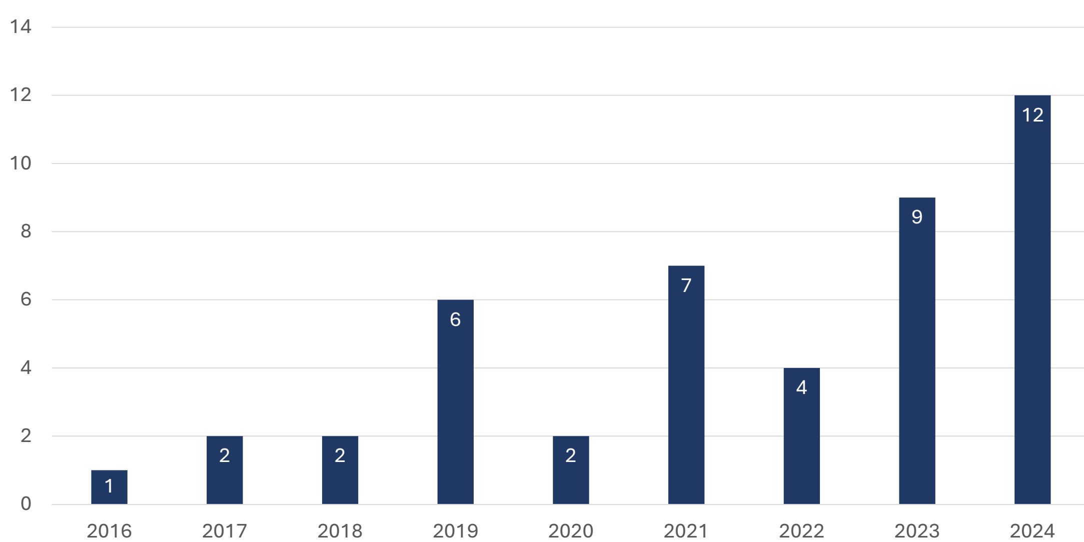
Trend of Events 2016-2024



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Mechanism of Tricuspid Valve Injury

- Most TV injuries (26; 58%) occurred during LP retrieval, recapture, or repositioning.
- Failure to recapture the device using the DC and/or manually pulling the device from the RV to RA were reported in a few cases.
- Tether entanglement, and injury during advancement of the delivery catheter (DC) from the right atrium to the right ventricle.

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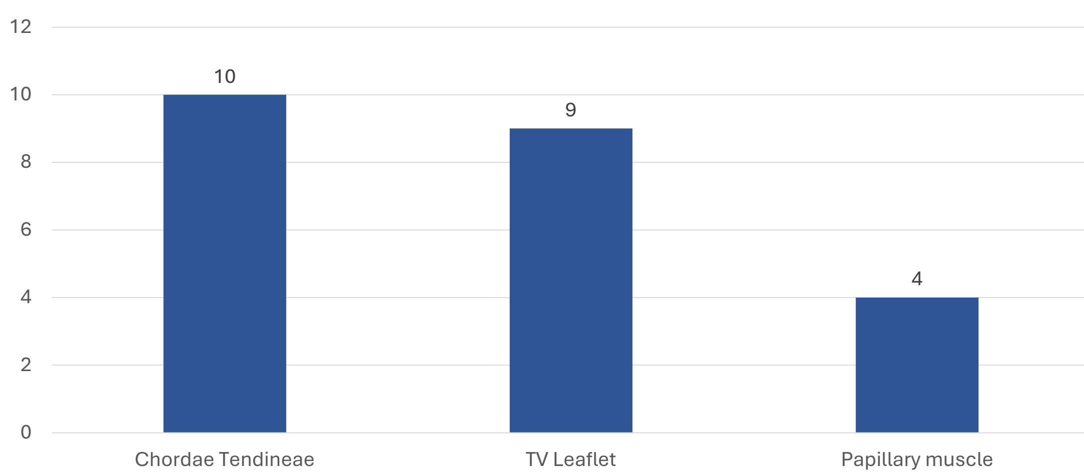
Tricuspid Valve Apparatus Injury Location



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Major Adverse Clinical Events

- Major adverse clinical events occurred in 16 (36%) patients.
- Death occurred in 5 (11%) patients, heart failure (n=5; 11%), and 10 patients (22%) required TV repair (4) or replacement (6).
- New or worsening TV regurgitation occurred in 30 (67%) cases.

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United States Reports

- There were a total of 14 procedure-related TV damage reports in the US.
- Micra VR; 8 events, Micra AV; 4 events, AVEIR VR; 2 events
- Crude US incidence was (14/149,287=0.01%) for all LPs.

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Limitations

- Our study is limited by its retrospective design as well as MAUDE's limitations, including underreporting.

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Conclusions

- TV damage is a major possible complication of LP implantation. Although rare, it can be associated with poor clinical outcomes and need for surgical valvular intervention.
- Possible mechanism for injury include TV damage during device recapture.
- Manufacturers should consider reporting TV complications in their product performance reports to increase the awareness among implanters.

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Procedure-related Tricuspid Valve Damage Associated with Implantation of Leadless Pacemakers. A MAUDE Database Study

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Background

- Micra™ and Aveir™ are two FDA-approved leadless pacemaker (LP) systems available worldwide.
- No tricuspid valve (TV) injuries were reported in their pivotal clinical trials. However, we and others have previously reported cases of TV injuries during Micra VR implantation.
- The aim of this study was to update the Micra experience and determine if Aveir VR implantation may also be associated with TV injury during LP implantation.

Methods

- In March 2025 we queried the FDA's Manufacturers and User Facility Device Experience (MAUDE) database with Basil system software (Boston MA).
- We searched for MAUDE reports involving Micra VR, Micra AV, and Aveir VR using the search term "tricuspid". Included were reports of procedure-related TV damage.
- Major adverse clinical events (MACE) included death, heart failure, or need for tricuspid valve repair or replacement.

Results

- We found 45 reports of procedure-related TV injuries associated with Micra (n=41; 91%) and Aveir (n=4; 9%) from centers worldwide.
- Most events (n=31; 69%) occurred outside the US. Median patient age was 81 (72,87) years and half were females (50%).
- Direct damage to the TV apparatus included the chordae tendineae (n=10), TV leaflets (n=9), and papillary muscles (n=4); 22 reports did not specify the injury location (Figure 1).

Figures and Tables

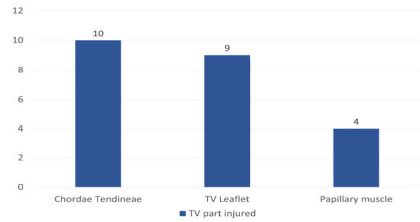

Figure 1. Specifying the injured parts of the tricuspid valve apparatus

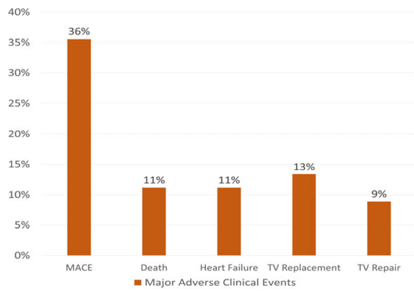

Figure 2. Percentage calculated relative to the total number of patients (45) included in the study

Results

- Most TV injuries (26; 58%) occurred during LP retrieval, recapture, or repositioning. Failure to recapture the device using the DC and/or manually pulling the device from the RV to RA were reported in 3 cases.
- Other injury mechanisms included tether entanglement, and injury during advancement of the delivery catheter (DC) from the right atrium to the right ventricle.
- Major adverse clinical events occurred in 16 (36%) patients including death (n=5; 11%), heart failure (n=5; 11%), and 10 patients (22%) required TV repair or replacement.
- New or worsening TV regurgitation occurred in 30 (67%) cases.
- LP removal was needed in 22 (44%) cases and one of these required surgery. A new LP was used as the replacement device in 14 (31%) cases, while TVPM was used in 3 (6.7%) cases

Conclusions

- Significant TV damage may complicate LP implantation regardless of the device model.
- TV damage is a major complication of LP implantation. Although probably rare, it is associated with poor clinical outcomes and need for surgical valvular intervention.
- Possible mechanisms for TV injury include TV damage during repositioning or retrieval. Also, injury during advancement of the DC through valve leaflet has been described.

Disclosures

The authors do not have any conflict of interest to disclose

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Thank you

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Lack of Calibration Degrades the Performance of Clinical Prediction Models: A Case of CTO Scores

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Disclosures

- None

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Motivation

- IIR statistics team reviewed all 6429 "Heart Failure Prediction" papers on PubMed
  - 212 build novel prediction models in humans
    - Only 83 papers demonstrated acceptable statistical standards
- We've built several risk prediction scores here
- Currently working on a risk prediction score with CCAD
  - Technical failure of CTO PCI procedure
- Comparison to past 4 scores revealed concerning inconsistency in risk classification

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Risk Score

- What is a risk score?
  - An equation/algorithm that transforms patient information into the probability of experiencing an event of interest
- How is it helpful?
  - Helps physicians make decisions
    - Should this patient stay in the hospital?
    - Which procedure should be used for the given patient? More or less invasive?
- What makes a risk score better or worse?
- How does one develop a better risk score?
  - TRIPOD Statement provides guidance

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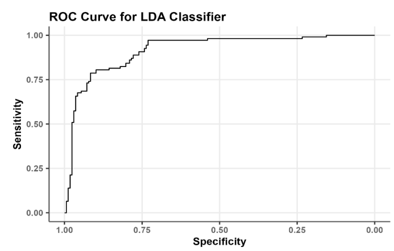
TRIPOD Recommendations

- Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis
- Recommendations regarding sample size, data separation, missing data handling, etc.
- Emphasis on how to measure and report model performance
- Two types of performance metrics:
  - Discrimination
  - Calibration
- Discrimination is well-reported
- Calibration is not



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Methods

- 7,872 CTO PCIs taken from PROGRESS-CTO Registry
  - Restricted to cites with 40+ CTO-PCIs
  - 13.6% technical failure rate
- Calibration was summarized using mean calibration and calibration slope then visualized via a calibration curve
- The calibration curves were estimated using penalized regression splines
- Mean calibration and calibration slopes were estimated from logistic regression models of the predicted probabilities on the true outcomes
- Score disagreement between scores was shown via a Sankey Diagram

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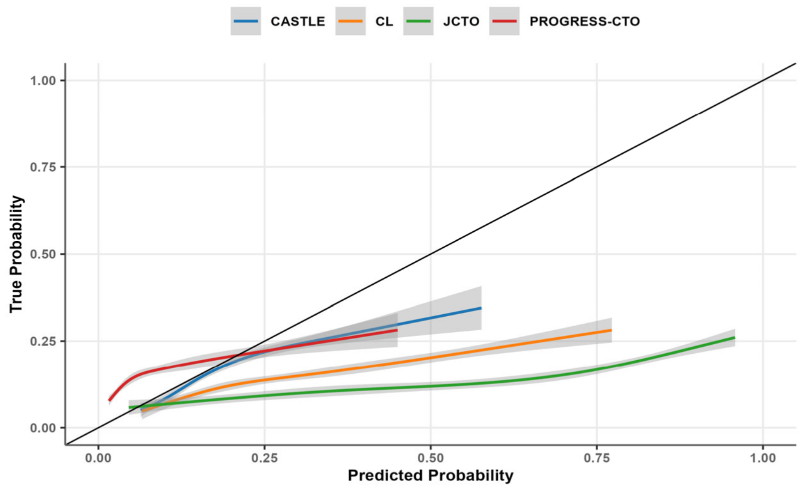
Results: Calibration Curves



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Score	AUC (Ideal=1)	Mean Calibration (Ideal=0)	Calibration Slope (Ideal=1)
PROGRESS-CTO	0.61 (0.59, 0.62)	-0.06 (-0.06, -0.05)	0.39 (0.33, 0.49)
J-CTO	0.63: (0.61, 0.65)	0.38 (0.37, 0.39)	0.31 (0.27, 0.36)
CL	0.63: (0.61, 0.64)	0.14 (0.13, 0.15)	0.49 (0.42, 0.56)
CASTLE	0.65: (0.64, 0.67)	0.02 (0.01, 0.03)	0.89 (0.78, 0.99)

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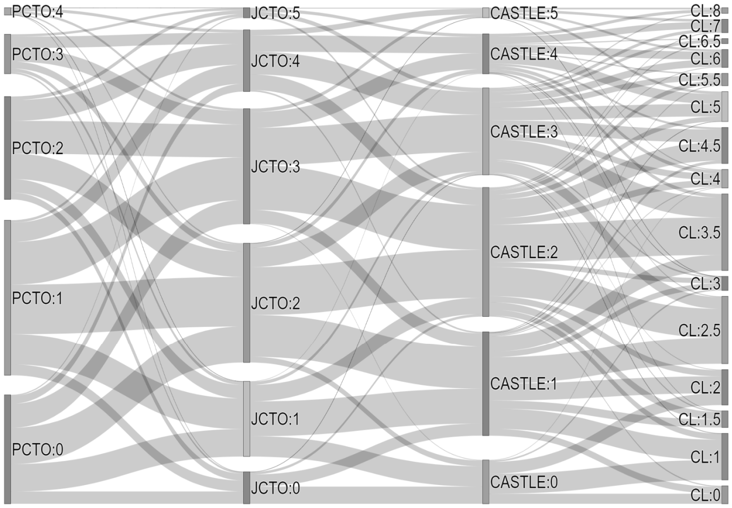
Disagreement in Risk Score Classification



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Conclusions

- All four CTO PCI risk prediction models show clear signs of miscalibration
- Despite being built using the same method with similar variables, the four scores disagree considerably on patient risk
- In the context of clinical decision-making, it is imperative to understand the predictions a model makes
- When building a risk scoring system, one should always show a model's calibration

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1. Collins GS, Dhiman P, Ma J, et al. Evaluation of clinical prediction models: from development to external validation. BMJ 2024.

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3. Collins GS, Reitsma JB, Altman DG, Moons KGM. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD statement. BMJ 2015.

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Questions?

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Creating a world without heart and vascular disease

The Use of Supersaturated Oxygen Therapy (SSO_2) in Patients with Late-Presentation Anterior STEMI

Paige Carlson, BS | Associate Research Coordinator & 2024 Lead Intern

Dr. Jay Traverse, MD | Physician Mentor

Sarah Schwager, RN & Katianna Feldewerd, BS | Staff Mentors

Seth Bergstedt, MS | Statistician

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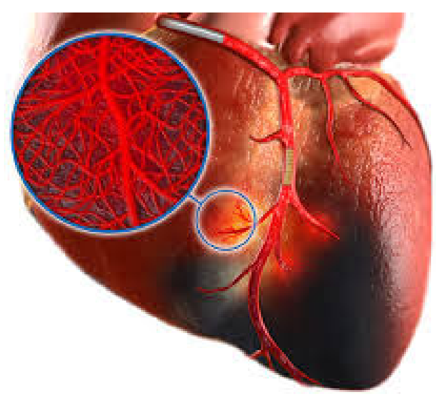
Objectives

- Background on ST-elevation myocardial infarctions (STEMIs), microvascular obstruction (MVO) and intramyocardial hemorrhage (IMH)
- Evidence and current indications for supersaturated oxygen (SSO_2) therapy
- **Research Question: Does SSO_2 therapy following PCI improve outcomes and microvascular injury in late-presentation anterior STEMI patients compared to routine primary PCI?**



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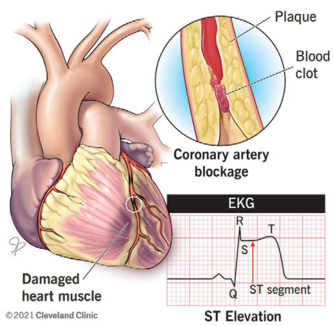
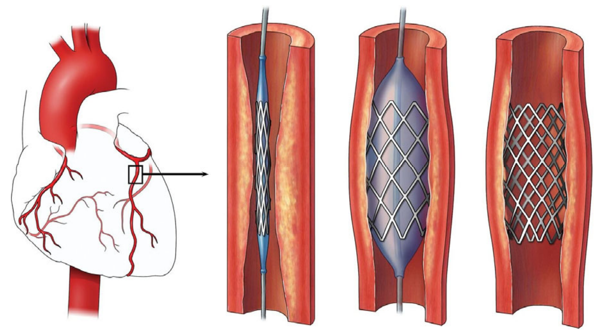
ST-Elevation Myocardial Infarction (STEMI)

- Estimated 280,000 STEMIs in the U.S. each year
- Symptoms: chest pain, shortness of breath, nausea, stomach discomfort
- Primarily treated via primary percutaneous coronary intervention (PCI)





https://my.clevelandclinic.org/-/scassets/images/org/health/articles/22068-stemi-heart-attack-illustration

https://images.squarespace-cdn.com/content/v1/5c9c8c17e3abc50001d21a1c/1570742231731-JF3XO5TPZ0ZHOVGRGLO9/angioplasty.jpg

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Late-Presentation STEMI

- Defined by amount of time between symptom onset and hospital arrival or intervention
- Associated with increased mortality and other adverse outcomes

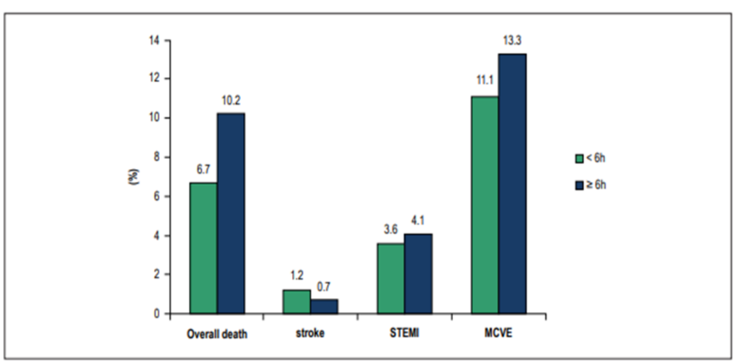
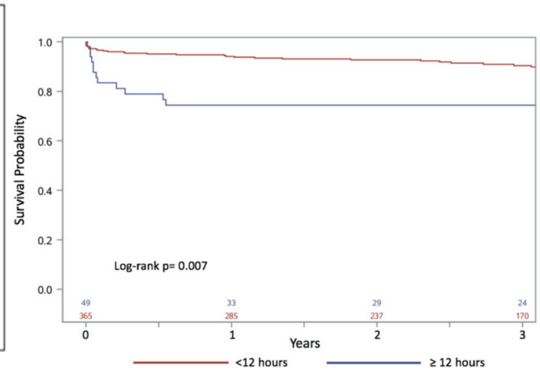


Figure 2 – *Clinical outcomes in 30 days. STEMI: acute ST-segment elevation myocardial infarction; MCVE: major cardiovascular events.*

Rodrigues et al., Arq Bras Cardiol 2018.



McNair, Bilchick & Keeley, Int J Cardiol Heart Vasc. 2019.

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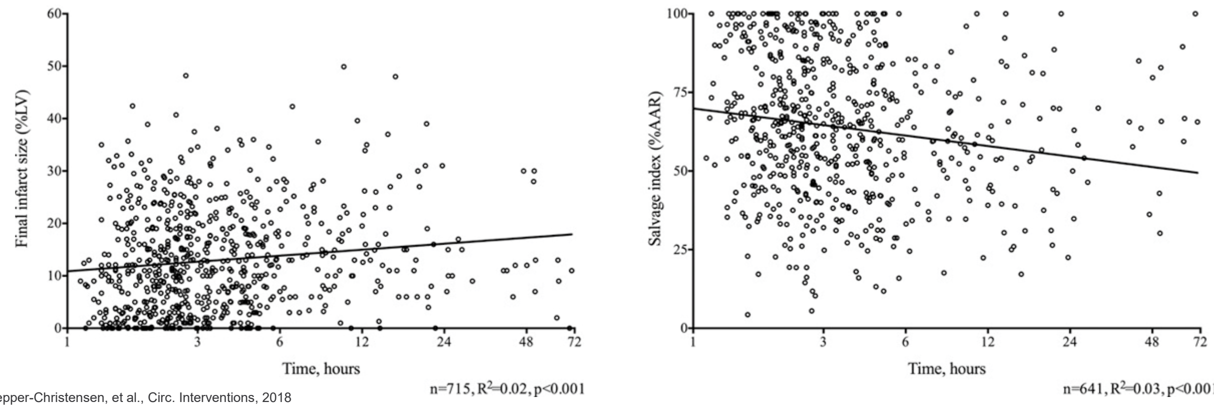
Risks for Late-Presenters

- Greater infarct size, decreased myocardial salvage
- At risk of MVO/IMH



Nepper-Christensen, et al., Circ. Interventions, 2018

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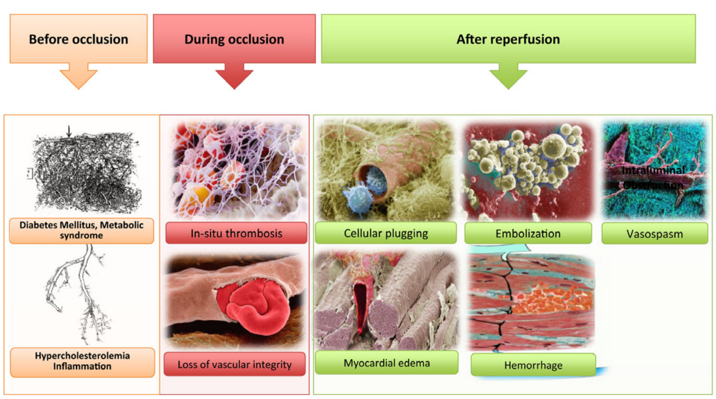
Microvascular Obstruction (MVO)

- Microvascular damage with “no-reflow” in area of infarct despite a patent coronary artery
- Several mechanisms, including extravascular compression from myocardial edema



Sezer et al JAHA 2018.

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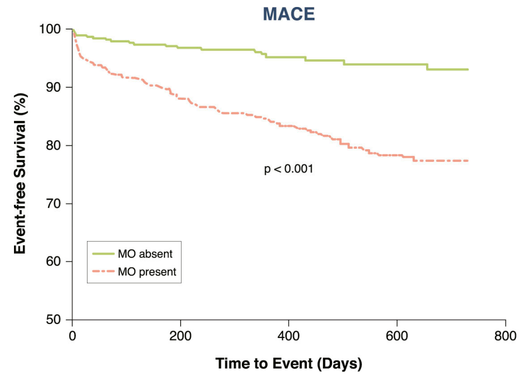
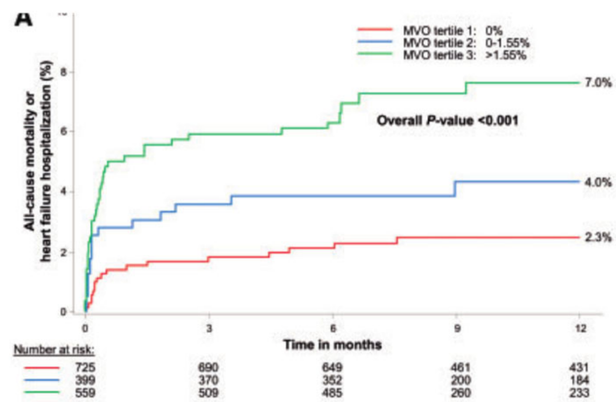
MVO & Adverse Events



Number at Risk					
MO absent	447	293	161	119	93
MO present	566	379	256	168	114

Van Kranenburg M, et al. JACC Imag. 2014



De Waha et al Eur Heart J 2017

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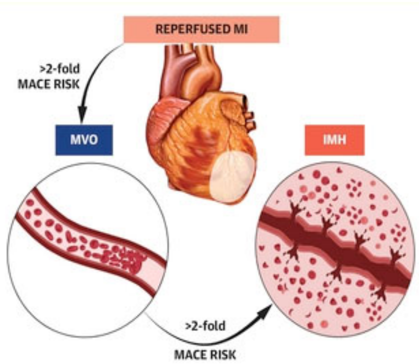
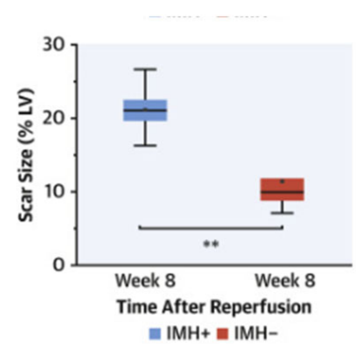
Intramyocardial Hemorrhage (IMH)

- Evolves from MVO and is caused by severe reperfusion injury in ischemic myocardium
- Associated with increased infarct size, adverse events, and mortality



Vora et al JACC Imaging 2024



Liu et al JACC 2022

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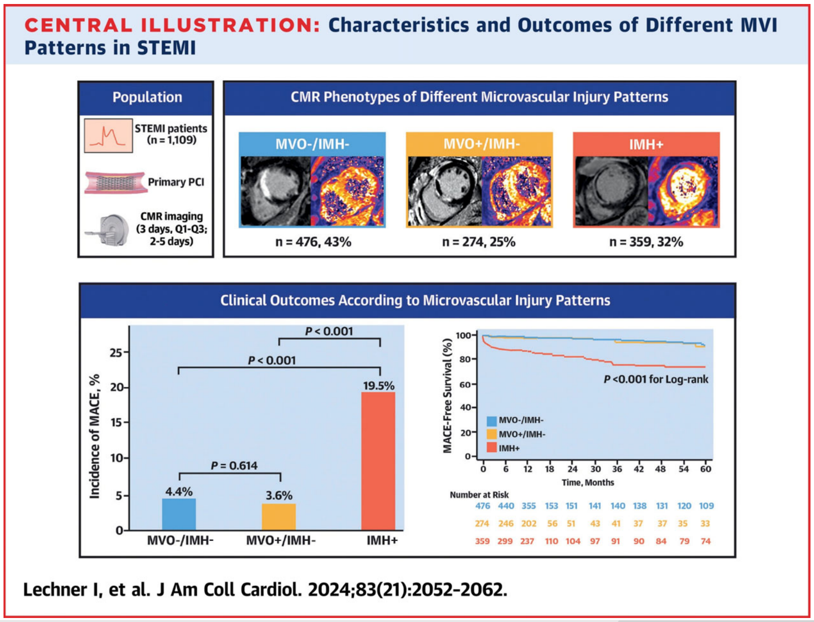

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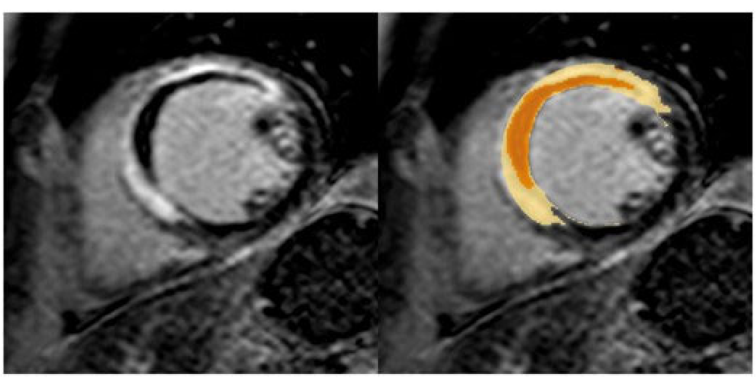
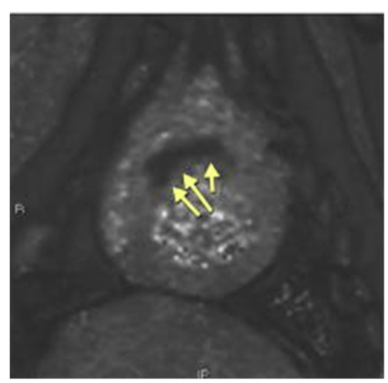
CMR Imaging of Infarct, MVO, and IMH

- Left: Late gadolinium enhancement (LGE) imaging shows infarct (yellow) and MVO (orange)
- Right: T2* imaging reveals presence of IMH (arrows) in porcine MI model



De Waha S., et al. Eur Heart J 2017



Hamirani et al JACC: Cardiovasc Imaging 2014

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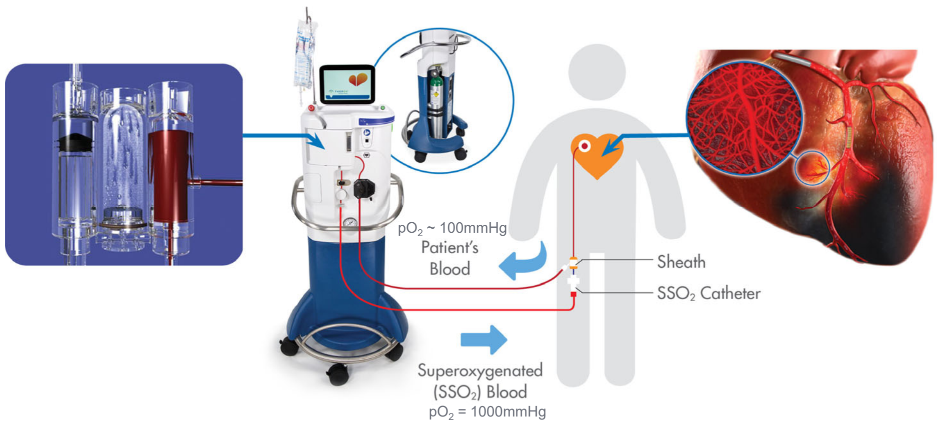
Supersaturated Oxygen Therapy (SSO_2)



https://www.zoll.com/-/media/opt/body-images/products/sso2_threapy/therox/ds2_ss02therapy_procedure_680x300_v3.ashx

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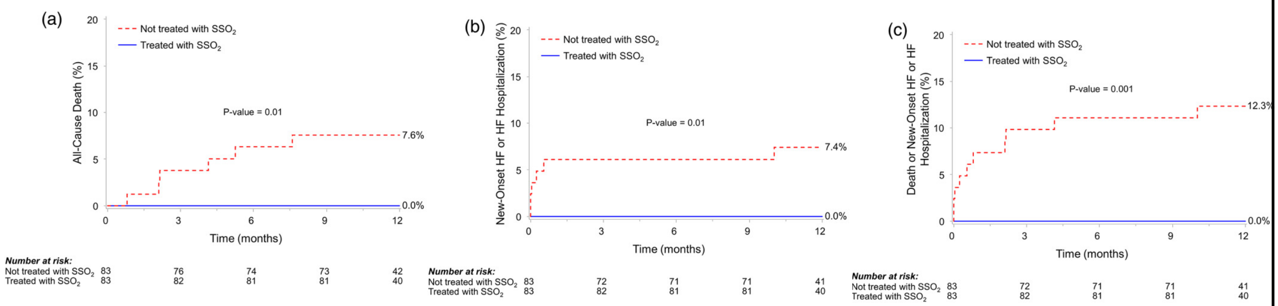
SSO_2 & Adverse Events

- Associated with a reduction in all-cause mortality, new-onset HF, HF hospitalization after 1 year
- Reduced infarct size and LV volumes



Chen et al., Catheter Cardiovasc Interv., 2020.

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SSO$_2$ & MVO

N= 874 Patients Qualified For Analysis

N = 90 in Treatment Group
IC-HOT and SSO$_2$ pilot study

N = 784 Patients in Control Untreated Group
7 Comparator Trials

Independent predictors of the extent of MVO

Covariate	Coefficient [95% CI]	Adjusted P value
SSO$_2$ (vs. no SSO$_2$)	-1.35 [-2.58, -0.11]	0.03
Age (per 5 years)	-0.16 [-0.31, 0.00]	0.054
Sex (male vs. female)	1.10 [0.29, 1.92]	0.008
Time from symptom onset to device (per 1 hour)	0.32 [0.06, 0.58]	0.02
Baseline TIMI flow grade ≤1 (versus ≥2)	2.08 [1.39, 2.76]	<0.0001

MVO in Patients Treated with SSO2 and Control Group

Characteristic	SSO2 group (N=90)	Control Group (N=784)	Unadjusted P value
Time to MVO assessment (days)	3.8 ± 1.2	3.6 ± 1.5	0.23
Extent of MVO (grams)	0.3 [0.0, 3.4]	1.1 [0.0, 5.2]	0.049
Percent MVO (%LV)	0.2 [0.0, 2.1]	0.8 [0.0, 3.8]	0.052
Any MVO Present	48/90 (53.3)	459/784 (58.5)	0.35
Infarct Size (%LV)	20.8 [10.5, 30.4]	24.7 [14.4, 37.3]	0.03

Falah et al., JSCAI, 2024.

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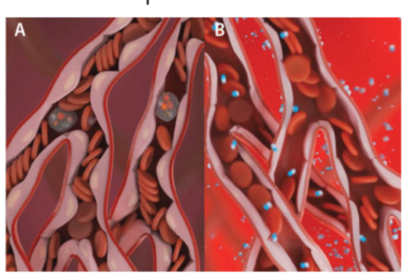
Current SSO$_2$ Indication

- Patients with an acute myocardial infarction in the left anterior descending (LAD) artery who present to the hospital within 6 hours of symptom onset
- Pre-clinical data in animals suggest that SSO$_2$ can be effective up to 24 hours from symptom onset
- However, a randomized, placebo-controlled trial of SSO$_2$ vs Control following STEMI using MRI imaging has never been performed



https://core4-cms.imgix.net/issue-2021/1021_FT_Fig1.png

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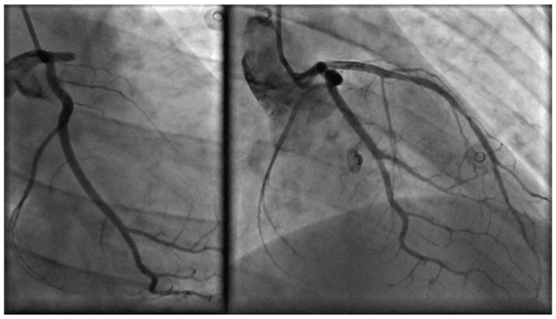
Research Question

Does supersaturated oxygen therapy (SSO_2) following PCI improve outcomes and microvascular injury in late-presentation anterior STEMI patients compared to routine primary PCI?



https://www.omicsonline.org/articles-images/2376-127X-2-183-g002.gif

https://info.zoll.com/hubfs/Assets%20Zoll%202022/images/Picture1.png

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Inclusion & Exclusion Criteria

Electronic search in Level One STEMI database – 840 patients with initial anterior STEMI from 2014-2024

→ 611 patients excluded: no cardiac MRI prior to discharge

229 patients received cardiac MRI prior to discharge

→ 179 patients excluded:
-171 patients: ischemic time (intermittent or <12 hours)
-6 patients: did not receive PCI
-1 patients: cardiac arrest
-1 patient: received LVAD

50 late-presentation anterior STEMIs included for analysis

- 19 patients received SSO2 therapy
- 31 control patients (no SSO2 therapy)

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Results: Patient Demographics

	All N=50	Control N=31	SSO_2 N=19	P-value
Age	60 (52, 73)	59 (50, 78)	60 (52, 66)	0.7
Male	31 (62%)	19 (61%)	12 (63%)	0.9
BMI	29.5 (25.6, 33.1)	27.9 (24.6, 31.8)	32.0 (27.4, 40.4)	**0.005**
White	43 (88%)	27 (90%)	16 (84%)	0.3
Hypertension	20 (40%)	12 (39%)	8 (42%)	0.8
Diabetes mellitus	16 (32%)	10 (32%)	6 (32%)	>0.9
Dyslipidemia	28 (58%)	13 (45%)	15 (79%)	**0.019**
Smoking				0.2
Current	13 (27%)	9 (30%)	4 (21%)	
Former	10 (20%)	8 (27%)	2 (11%)	
History of CAD	3 (6.0%)	1 (3.2%)	2 (11%)	0.5
Family history of CAD	10 (22%)	8 (31%)	2 (11%)	0.2

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Results: Patient Demographics

	All N=50	Control N=31	SSO_2 N=19	P-value
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Results: Hospital Admission

	All N=50	Control N=31	SSO_2 N=19	P-value
Infarct of LAD	50 (100%)	31 (100%)	19 (100%)	>0.9
Ischemic Time (hours)	15 (12, 24)	20.5 (12, 24)	14 (12, 24)	0.3
Killip Class				0.4
I	41 (82%)	25 (81%)	16 (84%)	
II	3 (6.0%)	3 (9.7%)	0 (0%)	
III/IV	6 (12%)	3 (9.7%)	3 (16%)	
Cardiogenic shock	5 (10%)	3 (9.7%)	2 (11%)	>0.9
Drug eluting stent	50 (100%)	31 (100%)	19 (100%)	>0.9
Medications at discharge				
ASA	46 (94%)	30 (97%)	16 (84%)	0.15
ACE/ARB	46 (94%)	28 (90%)	18 (95%)	0.9
Statin	49 (98%)	30 (97%)	19 (100%)	>0.9
Beta Blocker	47 (96%)	30 (97%)	17 (89%)	0.5

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Results: Procedural Characteristics

	All N=50	Control N=31	SSO_2 N=19	P-value
Initial Diameter Stenosis (%)	100 (99,100)	100 (99,100)	100 (100,100)	0.2
Initial TIMI Flow				0.4
0/1	38 (81%)	22 (76%)	16 (89%)	
2	9 (19%)	7 (24%)	2 (11%)	
3	0 (0%)	0 (0%)	0 (0%)	
Final Diameter Stenosis (%)	0 (0,0)	0 (0,0)	0 (0,0)	>0.9
Final TIMI Flow				>0.9
0/1	0 (0%)	0 (0%)	0 (0%)	
2	7 (15%)	4 (14%)	3 (17%)	
3	40 (85%)	25 (86%)	15 (83%)	
Procedure Time (min)	77 (30, 114)	34 (25, 54)	122 (114, 150)	**<0.001**
Thrombectomy	10 (20%)	8 (26%)	2 (11%)	0.3
Intra-aortic Balloon Pump Placement	7 (14%)	4 (13%)	3 (16%)	>0.9
Post-PCI ST-segment Elevation (mm)	1.33 (0.67, 1.67)	1.33 (1.00, 1.67)	0.92 (0.67, 1.33)	**0.018**

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Results: Procedural Characteristics

	All N=50	Control N=31	SSO_2 N=19	P-value
Initial Diameter Stenosis (%)	100 (99,100)	100 (99,100)	100 (100,100)	0.2
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3	0 (0%)	0 (0%)	0 (0%)	
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Final TIMI Flow				>0.9
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Results: cMRI Comparison

	All N=50	Control N=31	SSO_2 N=19	P-value
Baseline LVEF (%)	33 (33, 48)	33 (31, 44)	33 (33, 48)	0.50
Follow-Up LVEF (%)	43 (33, 53)	46 (33, 62)	44 (33, 53)	0.75
LVEDV (ml)	170 (142, 214)	159 (125, 216)	174 (155, 204)	0.3
LVESV (ml)	102 (72, 122)	91 (66, 122)	108 (84, 123)	0.3
LV Mass (g)	139 (115, 175)	133 (107, 177)	155 (118, 175)	0.4
Infarct Size (% of LV mass)	34 (25, 41)	34 (25, 41)	34 (24, 43)	>0.9
Presence of MVO	43 (91%)	31 (100%)	12 (75%)	**0.010**
MVO (% of LV Mass)	12 (9, 18)	12 (9, 19)	12 (3, 17)	0.3
Presence of IMH	26 (87%)	14 (100%)	12 (75%)	0.10

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Results: cMRI Comparison

	All N=50	Control N=31	SSO_2 N=19	P-value
Baseline LVEF (%)	33 (33, 48)	33 (31, 44)	33 (33, 48)	0.50
Follow-Up LVEF (%)	43 (33, 53)	46 (33, 62)	44 (33, 53)	0.75
LVEDV (ml)	170 (142, 214)	159 (125, 216)	174 (155, 204)	0.3
LVESV (ml)	102 (72, 122)	91 (66, 122)	108 (84, 123)	0.3
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Presence of IMH	26 (87%)	14 (100%)	12 (75%)	0.10

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Results: Outcomes

	All N=50	Control N=31	SSO_2 N=19	P-value
Death	7 (14%)	7 (23%)	0 (0%)	**0.035**
Reinfarction	3 (6.0%)	3 (9.7%)	0 (0%)	0.3
Stroke	2 (4.0%)	2 (6.5%)	0 (0%)	0.5
Cardiac Rehospitalization	20 (40%)	15 (48%)	5 (26%)	0.12
Revascularization	4 (8.0%)	4 (13%)	0 (0%)	0.3
MACE	6 (12%)	6 (19%)	0 (0%)	0.071

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Results: Outcomes

	All N=50	Control N=31	SSO_2 N=19	P-value
Death	7 (14%)	7 (23%)	0 (0%)	0.035
Reinfarction	3 (6.0%)	3 (9.7%)	0 (0%)	0.3
Stroke	2 (4.0%)	2 (6.5%)	0 (0%)	0.5
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Results: Outcomes

	All N=50	Control N=31	SSO_2 N=19	P-value
Death	7 (14%)	7 (23%)	0 (0%)	0.035
Reinfarction	3 (6.0%)	3 (9.7%)	0 (0%)	0.3
Stroke	2 (4.0%)	2 (6.5%)	0 (0%)	0.5
Cardiac Rehospitalization	20 (40%)	15 (48%)	5 (26%)	0.12
Revascularization	4 (8.0%)	4 (13%)	0 (0%)	0.3
MACE	6 (12%)	6 (19%)	0 (0%)	0.071

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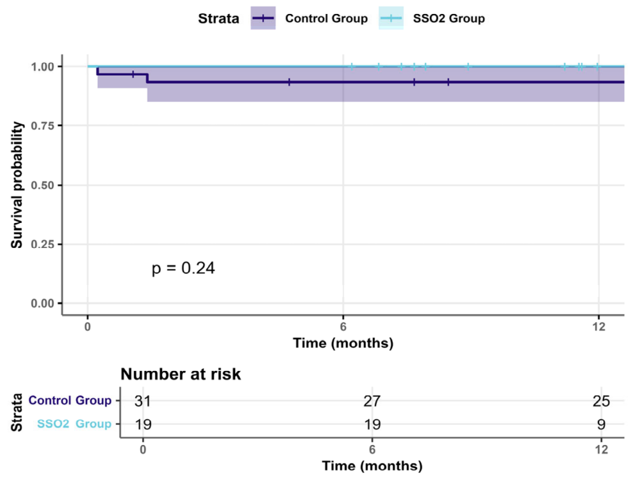
Survival free from major adverse CV events



Conclusions & Limitations

Conclusions

- SSO_2 can be safely delivered to late-presentation anterior STEMI patients and results in less microvascular injury as assessed by MVO and IMH.
- This translated to fewer CV adverse events and improved mortality in the SSO_2 treatment group.
- SSO_2 therapy may represent a new treatment for this high-risk patient group.

Next Steps

- Present our findings at ACC 2025 and publish manuscript
- Continue SSO_2 research and treatment for late-presenters

Limitations

- Small cohort size
- Retrospective chart review
- Single-center study limited to ANW Level One patients

Acknowledgments

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Lisa Tindell
Jenni Wagner

MHI/MHIF Team

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Questions?

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PROGRESS

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Trends of drug coated balloon use in chronic total occlusion percutaneous coronary intervention: Insights from the PROGRESS-CTO registry

March 24, 2025

Deniz Mutlu, MD

(on the behalf of the PROGRESS-CTO investigators)

Senior Research Scholar, Center for Coronary Artery Disease (CCAD),

Minneapolis Heart Institute Foundation

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Disclosure of Relevant Financial Relationships

I, Deniz Mutlu DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

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Background

Challenges of CTO PCI

- High rate of stent restenosis
- In-stent CTO
- Diffuse distal vessel stenosis
- Bifurcation CTO

Brilakis ES. Manual of CTO PCI, A Step-by-Step Approach, Academic press 2023

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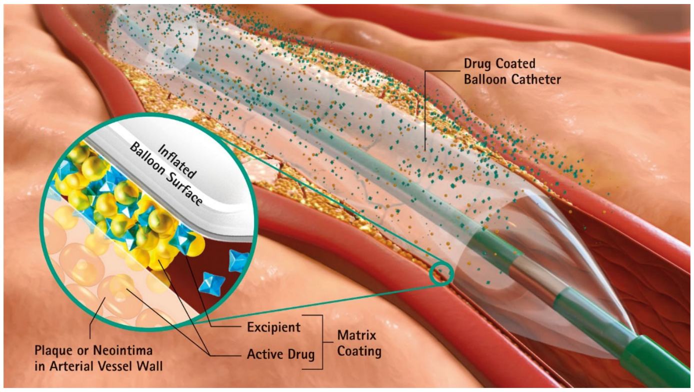
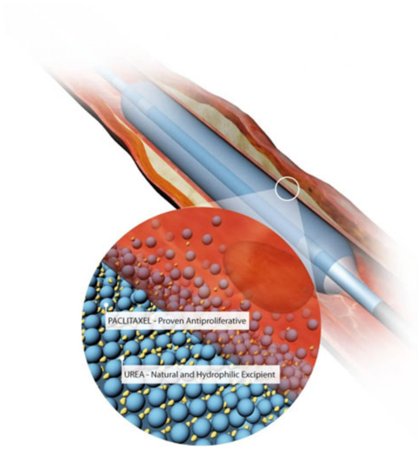
Background





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Jeger, R et al. Drug-Coated Balloons for Coronary Artery Disease: Third Report of the International DCB Consensus Group. J Am Coll Cardiol Intv. 2020,13:1391–1402.
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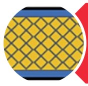
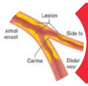
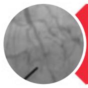
DCB indications in CTO PCI


In-stent CTO


De novo CTO


Investment procedure


Side branch treatment


Diffuse distal vessel disease

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Korjian et al. Circ Cardiovasc Interv. 2024;17:e013302.
Barrero Mier et al. JSCAI. 2022;1,5; 100466
Jun EJ et al. Front Cardiovasc Med. 2022,13;9:821380.

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Goal

- To examine the frequency of DCB utilization in an international registry

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Global Coordinating Center: Chairman/PI: E. S. Brilakis; **Global Director:** B.V. Rangan;
Database Managers: Dimitrios Strepkos, Deniz Mutlu, Michaella Alexandrou, Pedro Carvalho, Ozgur Selim Ser
Operational Support: Olga Mastrodemos
Project Impact: Data from 17,700 cases at 80 participating centers, 10 countries
Resulting in 138 publications, 201 conference presentations

PROGRESS CTO

NCT02061436

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Statistical analysis

- Categorical variables are presented as percentages and compared using Pearson's chi-square test or Fisher's exact test
- Continuous variables are presented as mean ± SD or as median (interquartile range [IQR]) and compared using the Student's t-test and the Mann-Whitney U test
- Time trend analysis was assessed using Mann-Kendall test for Monotonic trend
- A 2-sided p value of 0.05 was considered to indicate statistical significance

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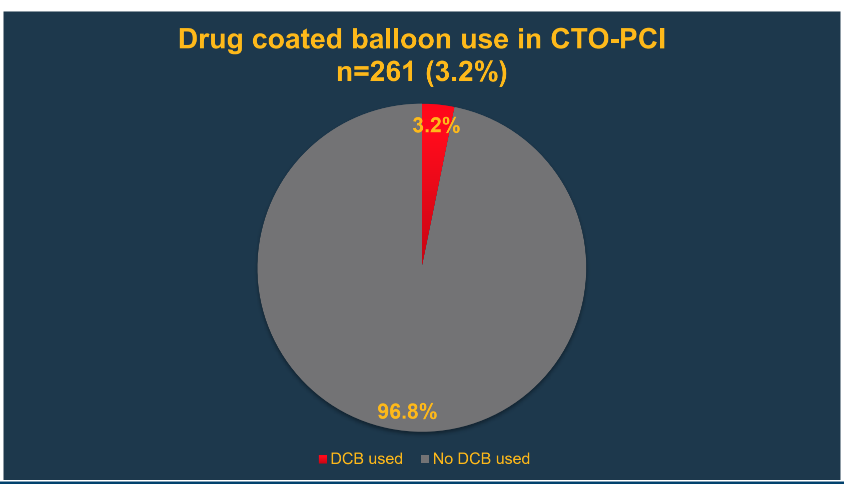
Results

- 8238 CTO PCIs performed between 2018 and 2024 at 43 centers



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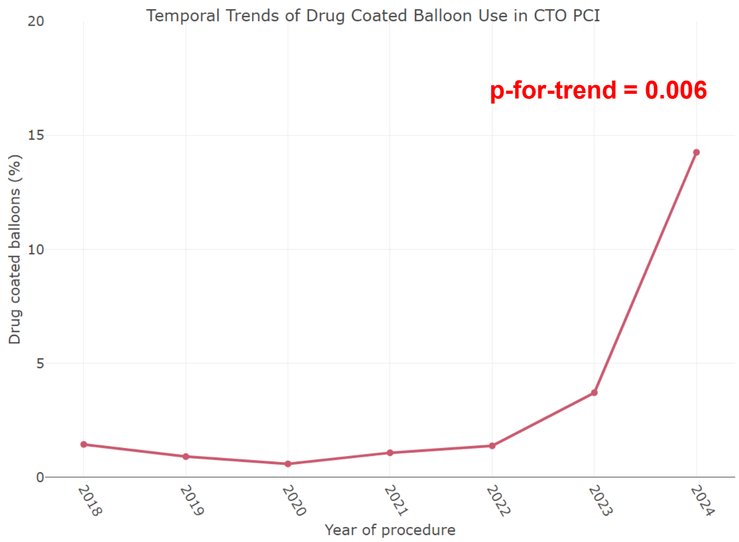
Increase of DCB use between 2018 and 2024



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Patients with DCB had less comorbidities

Variable	DCB used (n=257)	No DCB used (n=7969)	P value
Age	61 ± 12	64 ± 10	**<0.001**
Male gender	81.6%	80.0%	0.585
Diabetes mellitus	43.9%	51.6%	**0.018**
Hypertension	75.8%	85.8%	**<0.001**
LVEF (%)	51.5 ± 10.4	50.6 ± 12.4	0.267
Prior heart failure	13.2%	26.5%	**<0.001**
Prior MI	38.9%	41.8%	0.410
Prior CABG	17.5%	24.6%	**0.013**
Cerebrovascular disease	4.9%	9.2%	**0.025**
Peripheral arterial disease	5.3%	13.1%	**<0.001**

CABG: coronary artery bypass grafting; DCB: drug coated balloon; LVEF: left ventricular ejection fraction; MI: myocardial infarction; PCI: percutaneous coronary intervention.

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Intravascular imaging was used more frequently in patients with DCB used

Variable	DCB used (n=257)	No DCB used (n=7969)	P value
CAD presentation			**<0.001**
Stable angina	74.8%	67.4%	
Unstable angina	8.7%	15.5%	
NSTEMI	2.4%	7.2%	
STEMI	0.8%	1.2%	
Baseline creatinine (mg/dl)	0.95 (0.80-1.09)	1.00 (0.80-1.20)	**0.001**
Intravascular imaging	58.9%	50.0%	**0.006**

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CAD: coronary artery disease; DCB: drug coated balloon; NSTEMI: Non-ST segment elevation myocardial infarction; STEMI: ST segment elevation myocardial infarction.

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Complex lesion characteristics were less common in the DCB patients

Variable	DCB used (n=261)	No DCB used (n=7977)	P value
CTO Target vessel			0.231
RCA	47.5%	52.2%	
LAD	32.2%	27.1%	
LCX	17.3%	18.4%	
Other	3.1%	2.3%	
Vessel diameter (mm)	3.0 ± 0.5	3.1 ± 0.6	**0.001**
Occlusion length (mm)	31.3 ± 17.8	30.5 ± 20.7	0.558
Proximal cap ambiguity	26.7%	33.3%	**0.037**
Blunt/no stump	43.2%	50.1%	**0.034**
Calcification (moderate/severe)	35.9%	41.8%	0.066
Tortuosity (moderate/severe)	19.8%	25.6%	**0.041**
J-CTO score	2.1 ± 1.2	2.3 ± 1.2	**0.007**
PROGRESS-CTO score	1.1 ± 0.9	1.2 ± 1.0	0.339

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CTO: chronic total occlusion; J: Japan; LAD: left anterior descending; LCX: left circumflex; PROGRESS-CTO: prospective global registry for the study of chronic total occlusion intervention; RCA: right coronary artery.

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Retrograde strategy was less frequent in DCB patients

Variable	DCB used (n=261)	No DCB used (n=7981)	P value
First crossing strategy			0.150
Antegrade wiring	90.4%	85.7%	
ADR	1.9%	2.0%	
Retrograde	7.4%	11.1%	
Retrograde strategy used	22.6%	28.6%	**0.040**
ADR strategy used	12.3%	16.4%	0.089
Successful strategy			**0.005**
Antegrade wiring	70.7%	61.6%	
ADR	7.7%	11.5%	
Retrograde	17.8%	18.5%	
None	3.9%	8.5%	

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ADR: antegrade dissection and re-entry.

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ISR CTO were more frequent in DCB patients

Variable	DCB used (n=261)	No DCB used (n=7981)	P value
Balloon uncrossable lesion	5.5%	8.3%	0.135
Balloon undilatable lesion	4.7%	5.8%	0.582
ISR CTO	42.9%	15.6%	**<0.001**
Number of stent used	1.6 ± 0.8	2.2 ± 1.0	**<0.001**
Procedure time (min)	99 (66-131)	106 (72-154)	**0.047**
Contrast volume (ml)	222 (150-300)	190 (130-265)	**<0.001**
Fluoroscopy time (min)	40 (25-60)	40 (25-62)	0.918

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CTO: chronic total occlusion; DCB: drug coated balloon; ISR: in-stent restenosis.

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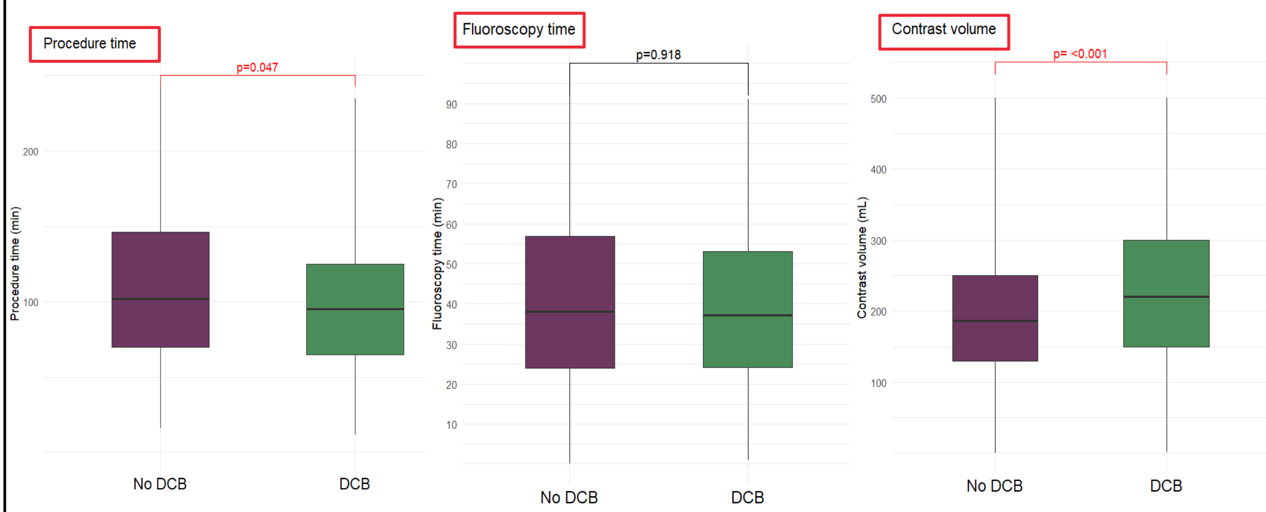
Procedure time was lower in DCB patients



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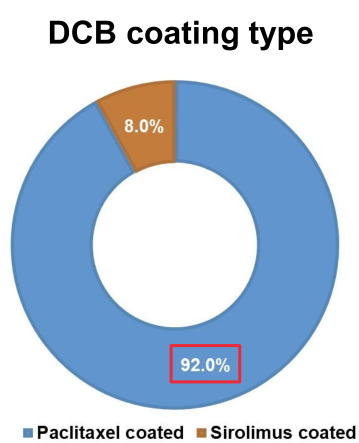
Paclitaxel coated DCB was frequently used

Variable	DCB used (n=261)
Number of DCB used	1.3 ± 0.6
DCB diameter, mm	3.3 ± 2.1
DCB length, mm	33.5 ± 15.8
DCB strategy	
Only DCB	53.7%
Hybrid (DCB+ DES)	46.3%
Reason for DCB use	
In-stent CTO	42.9%
Investment procedure	30.7%
Side branch treatment	13.7%
Diffuse distal vessel disease	9.8%
Bail-out stenting required	2.9%



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CTO: chronic total occlusion; DCB: drug coated balloon; DES: drug eluting stent.

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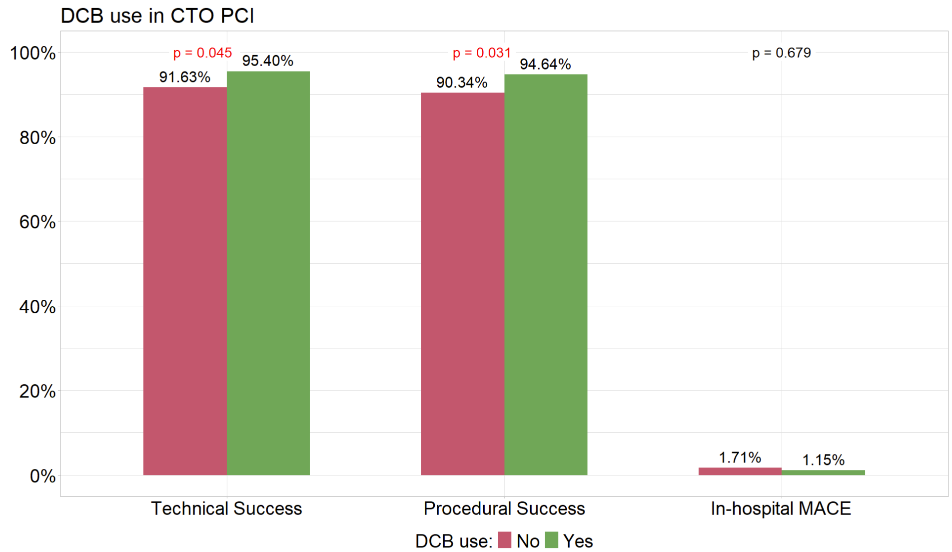
Better outcomes with DCB use



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MACE: major adverse cardiovascular events.

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Limitations

- Observational study with all inherent limitations
- No core laboratory analysis of the angiograms
- PROGRESS-CTO registry: experienced operators in performing CTO PCI, potentially limiting the external validity of the study's results.

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Conclusions

DCB are **increasingly** being **used** in CTO PCI and are associated with **high success** and **low complication** rates.

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Thank you!

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Mutlu D, Alexandrou M, Strepkos D, Carvalho PEP, Ser OS, Goktekin O, Jaffer FA, Frizzel J, Elbarouni B, Khatri JJ, Alaswad K, Davies R, Ozdemir R, Uluganyan M, Elguindy A, Ahmed Y, Choi JW, Young L, Basir M, Raj L, Azzalini L, Ybarra L, Riley R, Murad B,, Mastrodemos OC, Rangan BV, Sandoval Y, Burke MN, Gorgulu S, Brilakis ES.

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PROGRESS CTO

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PROGRESS

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Bifurcation percutaneous coronary intervention in octogenarians and nonagenarians: insights from the PROGRESS-BIFURCATION registry

March 24, 2025

Ozgur Selim Ser, MD

(on the behalf of the PROGRESS-BIFURCATION investigators)

Volunteer Research Scholar, Center for Coronary Artery Disease (CCAD),

Minneapolis Heart Institute Foundation

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Disclosure of Relevant Financial Relationships

I, Ozgur Selim SER DO NOT have any financial relationships to disclose.

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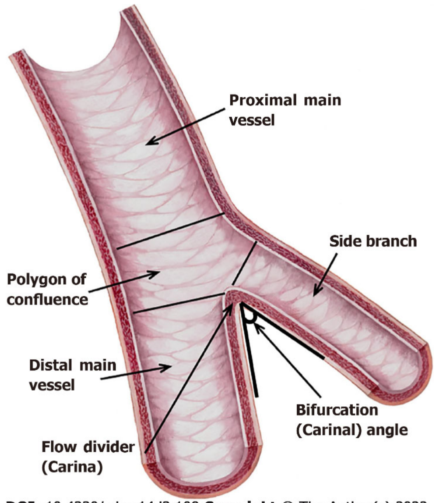
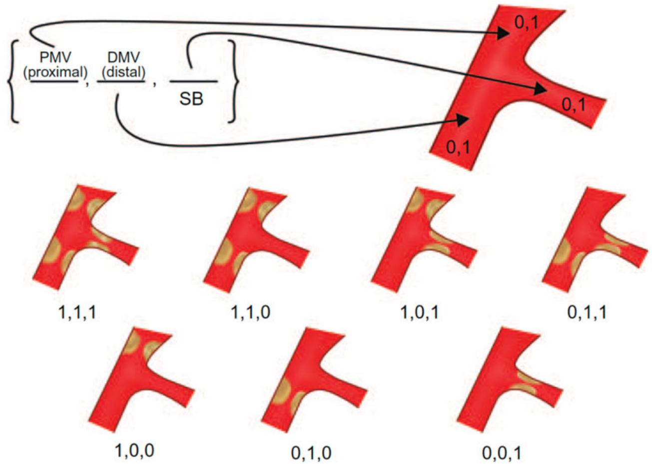
Background



DOI: 10.4330/wjc.v14.i3.108 **Copyright** © The Author(s) 2022.



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Brilakis ES. Manual of percutaneous coronary interventions. Academic press 2021
Kirat T. et al Fundamentals of percutaneous coronary bifurcation interventions.

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Background

- The life expectancy of individuals is increasing on a global scale.
- As the proportion of elderly individuals rises, the incidence of coronary artery disease rises as well.
- Coronary artery disease (CAD) is a significant cause of morbidity and mortality in individuals ≥80 years of age.
- However, elderly patients have generally been poorly represented in cardiovascular studies.

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Tsao CW, et al. Heart Disease and Stroke Statistics-2022 Update: A Report From the American Heart Association. *Circulation* 2022;145:e153-e639. Madhavan MV, Gersh BJ, Alexander KP, et al. . Coronary Artery Disease in Patients ≥80 Years of Age. *J Am Coll Cardiol* 2018;71:2015-2040.

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Goal

- To examine the outcomes of bifurcation percutaneous coronary intervention in ≥80-year-old patients in a large multicenter registry.

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Global Coordinating Center: Chairman/PI: E. S. Brilakis; **Global Director:** B.V. Rangan;
Database Managers: Dimitrios Strepkos, Deniz Mutlu, Michaella Alexandrou, Pedro Carvalho, Ozgur Selim Ser
Operational Support: Olga Mastrodemos
Project Impact: Data from 1768 cases at 7 participating centers, 3 countries

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Methods

- We analyzed the clinical and angiographic records of 1,253 patients who underwent bifurcation PCI comparing octogenarians and nonagenarians vs. younger patients in a multicenter registry between 2014 and 2024.

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Statistical analysis

- Categorical variables are presented as percentages and compared using Pearson's chi-square test or Fisher's exact test
- Continuous variables are presented as mean ± SD or as median (interquartile range [IQR]) and compared using the Student's t-test and the Mann-Whitney U test
- A 2-sided p value of 0.05 was considered to indicate statistical significance

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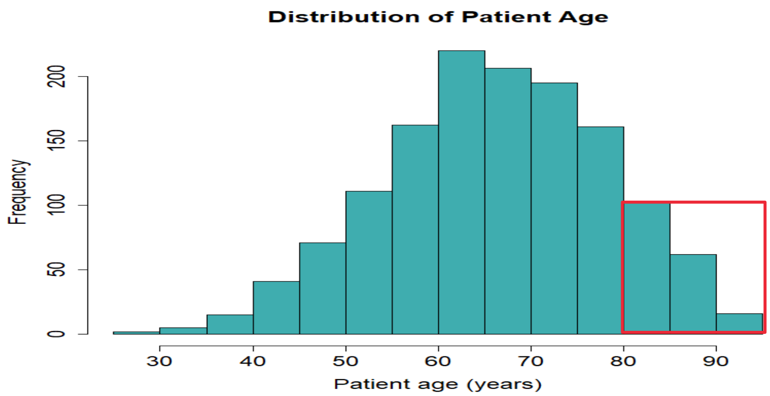
Results

- Of 1,253 patients undergoing bifurcation PCI, 194 (15%) were octogenarians or nonagenarians.



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Octogenarians/nonagenarians had more comorbidities

Variables	<80-years-old (n = 1060)	≥80-years-old (n = 193)	p-value
Age (years)	63.44 ± 9.82	84.32 ± 3.66	**<0.001**
Gender, male	75.8% (803)	66.8% (129)	**0.009**
BMI	30.70 ± 6.23	28.39 ± 5.58	**<0.001**
Hypertension	76.5% (811)	90.7% (175)	**<0.001**
Dyslipidemia	76.9% (815)	85.0% (164)	**0.012**
Smoking, current	22.8% (242)	1.0% (2)	**<0.001**
Diabetes mellitus	35.0% (371)	37.3% (72)	0.544
Left ventricular ejection fraction (%)	53.95 ± 12.68	52.21 ± 13.88	0.122
Family history of CAD	20.5% (210)	12.6% (24)	**0.011**
Heart failure	19.0% (201)	39.4% (76)	**<0.001**
Cerebrovascular disease	10.0% (106)	22.3% (43)	**<0.001**
Atrial fibrillation	11.8% (122)	29.8% (57)	**<0.001**
Baseline creatinine (mg/dL)	0.97 [0.81, 1.13]	1.10 [0.89, 1.36]	**<0.001**

BMI = body mass index; CAD = coronary artery disease

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Angiographic characteristic of study patients

Variables	<80-years-old (n = 1068)	≥80-years-old (n = 194)	p-value
Radial access used	48.0% (325)	32.4% (36)	**0.002**
LM stenosis (%)	0.00 [0.00, 30.00]	40.00 [10.00, 70.00]	**<0.001**
Proximal LAD stenosis (%)	70.00 [26.25, 90.00]	80.00 [60.00, 90.00]	**<0.001**
Ostial lesion (within 5 mm of aortocoronary ostium)	8.2% (86)	14.1% (27)	**0.009**
Proximal main vessel			**<0.001**
LM	22.8% (243)	45.6% (88)	
LAD	43.2% (460)	36.8% (71)	
RCA	15.3% (163)	5.2% (10)	
Circumflex	16.9% (180)	11.4% (22)	
Bypass graft	1.7% (18)	1.0% (2)	

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LM = Left main; LAD = Left anterior descending; CIRC = Circumflex; OM = Obtuse marginal; LPDA = Left posterior descending artery; LPL = Left posterolateral; RCA = Right coronary artery; RPDA = Right posterior descending artery; RPL = Right posterolateral; IVUS = Intravascular ultrasound; OCT = Optical coherence tomography

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Intravascular imaging was used more frequently in patients with octogenarians/nonagenarians

Variables	<80-years-old (n = 1068)	≥80-years-old (n = 194)	p-value
Proximal main vessel diameter (mm)	3.50 [3.00, 4.00]	3.50 [3.25, 4.00]	**<0.001**
Proximal main vessel diameter stenosis (%)	70.00 [40.00, 90.00]	70.00 [50.00, 90.00]	0.643
Distal main vessel diameter (mm)	3.00 [2.75, 3.25]	3.00 [2.76, 3.50]	**0.004**
Distal main vessel diameter stenosis (%)	80.00 [60.00, 90.00]	87.50 [70.00, 90.00]	0.565
Side branch diameter (mm)	2.50 [2.25, 2.80]	2.50 [2.25, 3.00]	**<0.001**
Side branch diameter stenosis (%)	60.00 [20.00, 90.00]	80.00 [30.00, 90.00]	**0.044**
Pretreatment IVUS/OCT	19.7% (209)	25.9% (50)	**0.049**

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IVUS = Intravascular ultrasound; OCT = Optical coherence tomography

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Complex lesion characteristics were more common in the octogenarians/nonagenarians

Variables	<80-years-old (n = 1068)	≥80-years-old (n = 194)	p-value
Proximal main vessel tortuosity			**0.041**
Straight (< 70 degrees, 1 Bend)	54.4% (581)	64.4% (125)	
Slight (>70 degrees, 1 Bend)	25.7% (274)	20.6% (40)	
Moderate (2 Bends >70 degrees or 1 Bend >90 degrees)	15.4% (164)	9.8% (19)	
Severe (2 Bends >90 degrees or 1 Bend >120 degrees)	4.6% (49)	5.2% (10)	
Calcification			**<0.001**
None	35.6% (380)	10.3% (20)	
Mild (Spots)	31.1% (332)	21.6% (42)	
Moderate (<=50% Reference Lesion Diameter)	19.3% (206)	29.9% (58)	
Severe (>50% Reference Lesion Diameter)	14.0% (149)	38.1% (74)	
Medina classification			0.089
1,1,1	38.9% (415)	50.0% (97)	
1,1,0	20.1% (215)	18.0% (35)	
1,0,1	5.0% (53)	4.6% (9)	
0,1,1	11.3% (121)	9.3% (18)	
1,0,0	8.2% (88)	6.2% (12)	
0,1,0	12.5% (133)	7.2% (14)	
0,0,1	3.9% (42)	4.6% (9)	

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Plaque modification was used more frequently in patients with octogenarians/nonagenarians

Variables	<80-years-old (n = 1068)	≥80-years-old (n = 194)	p-value
Side branch PTCA	32.9% (351)	47.9% (93)	**<0.001**
Provisional to two-stent conversion	6.0% (64)	6.2% (12)	0.917
Plaque modification use	39.0% (417)	53.1% (103)	**<0.001**
Number of stents for main vessel	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)	0.574
Number of stents for side branch	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)	0.445
Reason for IVUS use			0.318
Stent optimization	65.5% (165)	74.3% (52)	
Stent sizing	24.2% (61)	20.0% (14)	
To guide wiring	10.3% (26)	5.7% (4)	
Reason for OCT use			0.383
Stent optimization	75.0% (18)	75.0% (3)	
Stent sizing	20.8% (5)	0.0% (0)	
To guide wiring	4.2% (1)	25.0% (1)	

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PTCA = percutaneous transluminal coronary angioplasty, IVUS = Intravascular ultrasound, OCT = Optical coherence tomography.

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Octogenarians/nonagenarians associated with similar technical success but higher in-hospital and follow-up MACE and death

Variables	<80-years-old (n = 1060)	≥80-years-old (n = 193)	p-value
Procedural success	92.0% (975)	87.0% (168)	**0.026**
Technical success	95.0% (1,015)	93.3% (181)	0.317
Provisional stenting	68.2% (728)	57.2% (111)	**0.003**
Two-stent techniques	29.6% (316)	41.2% (80)	**0.001**
MACE	3.4% (36)	8.3% (16)	**0.002**
Death	1.0% (11)	3.1% (6)	**0.035**
Acute MI	1.4% (15)	3.1% (6)	0.119
Repeat PCI	1.2% (13)	2.1% (4)	0.316
Stroke	0.5% (5)	1.6% (3)	0.111
Emergency CABG	0.0% (0)	1.0% (2)	**0.024**
Bleeding	0.5% (5)	1.6% (3)	0.111
Side branch occlusion	0.1% (1)	0.0% (0)	>0.999
Contrast volume, ml	170.00 (130.00, 220.00)	150.00 (110.00, 200.00)	**0.011**
Fluoroscopy time	20.00 (12.90, 32.63)	23.50 (15.00, 35.10)	**0.007**
Air Kerma radiation dose (Gray)	1.39 (0.92, 2.12)	1.17 (0.77, 2.00)	**0.015**
Procedure time	75.00 (50.07, 117.40)	86.63 (60.00, 129.00)	**0.006**

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CABG = coronary artery bypass graft; MACE = major adverse cardiac events; MI = myocardial infarction; PCI = percutaneous coronary intervention

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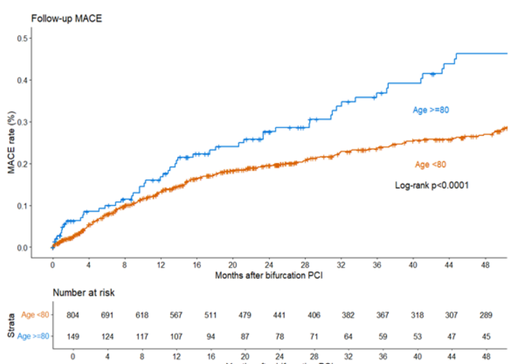
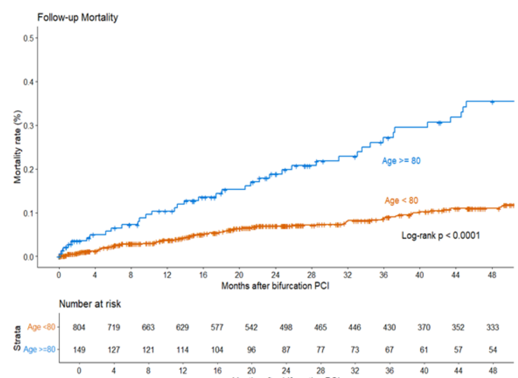
In Kaplan Meier analysis, octogenarians/nonagenarians had higher follow-up MACE and follow-up death





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MACE: major adverse cardiovascular events, PCI = percutaneous coronary intervention

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In multivariable analysis follow-up MACE was independently associated with age

Variables	Multivariate		
	HR	(95% CI)	p
Octo- and nonagenarians	1.462	1.047-2.041	0.026
Gender, male	0.834	0.628-1108	0.21
Diabetes mellitus	1.619	1.228-2.134	0.001
Hypertension	1.28	0.860-1.905	0.22
Heart failure	1.362	1.01-1.838	0.043
Chronic kidney Disease	1.495	1.097-2.036	0.011
Prior PCI	1.652	1.257-2.170	0.001
Proximal main vessel tortuosity	1.365	0.995-1.872	0.054
Moderate/severe calcification	1.353	0.963-1.901	0.082
LMCA lesion	1.511	1.043-2.19	0.029
Two-stent techniques	0.931	0.690-1.258	0.64

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Limitations

- Observational study with all inherent limitations
- No core laboratory analysis of the angiograms were present.
- Frailty was not evaluated.
- The possible enhancement of quality-of-life following bifurcation PCI was not evaluated. In elderly patients, quality of life indicators, such as relief of angina pectoris, may hold greater significance than survival extension.
- Procedures were conducted at high-volume, experienced PCI centers, potentially reducing the generalizability of our findings to less experienced centers.

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Conclusions

Bifurcation PCI in octogenarians and nonagenarians is associated with similar **technical success** but higher **in-hospital and follow-up MACE and mortality** compared with younger patients, likely related to a higher prevalence of **baseline comorbidities and higher complexity** of bifurcation lesions.

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Thank you!

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