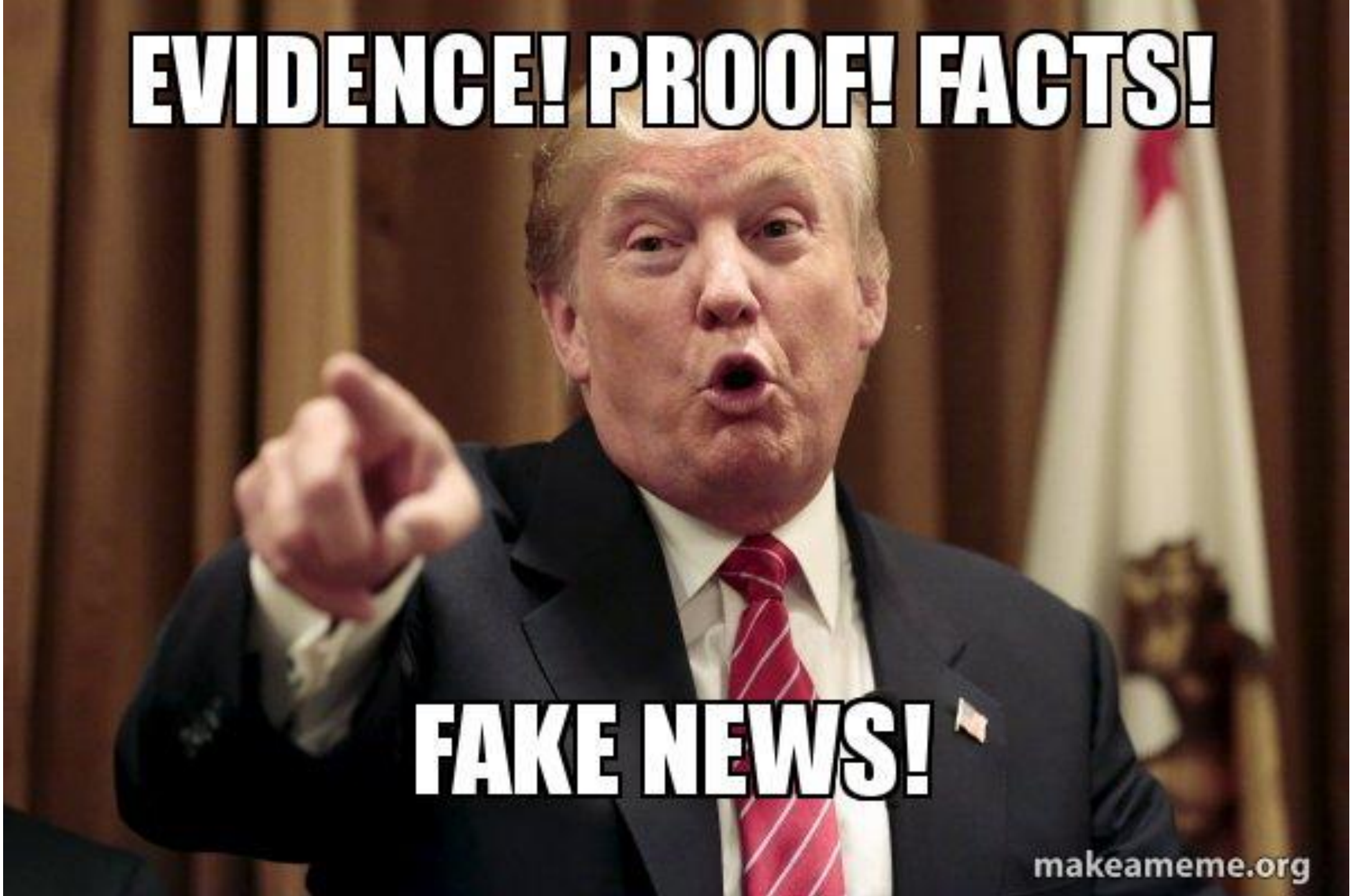
Management of no-reflow: Still an unsolved problem?

Ronen Jaffe, MD
Carmel Medical Center, Haifa, Israel


EVIDENCE! PROOF! FACTS!
FAKE NEWS!
makeameme.org

Epicardial coronary

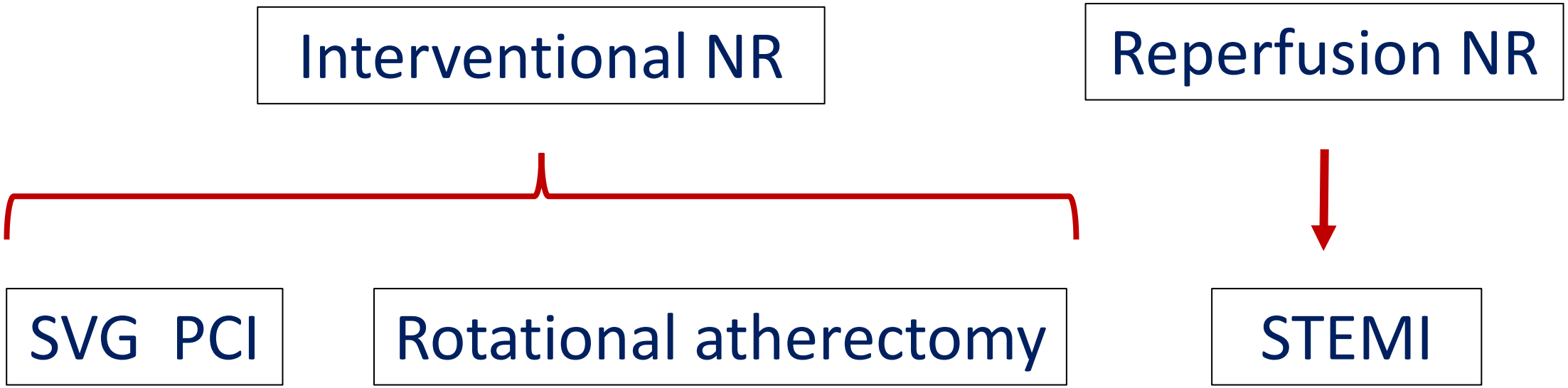
Microvascular network

Camici J Nucl Med 2009;50:1076

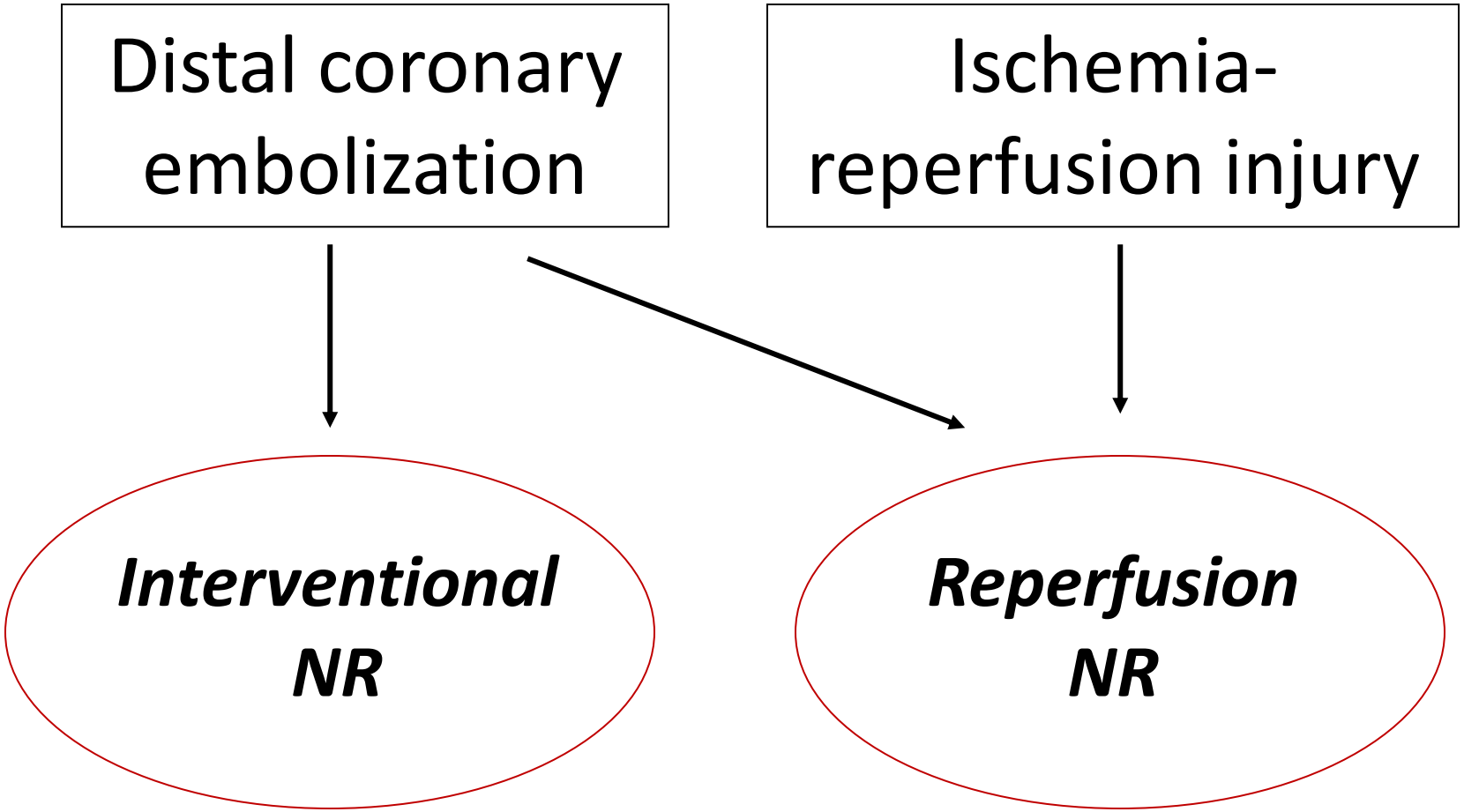
No reflow:

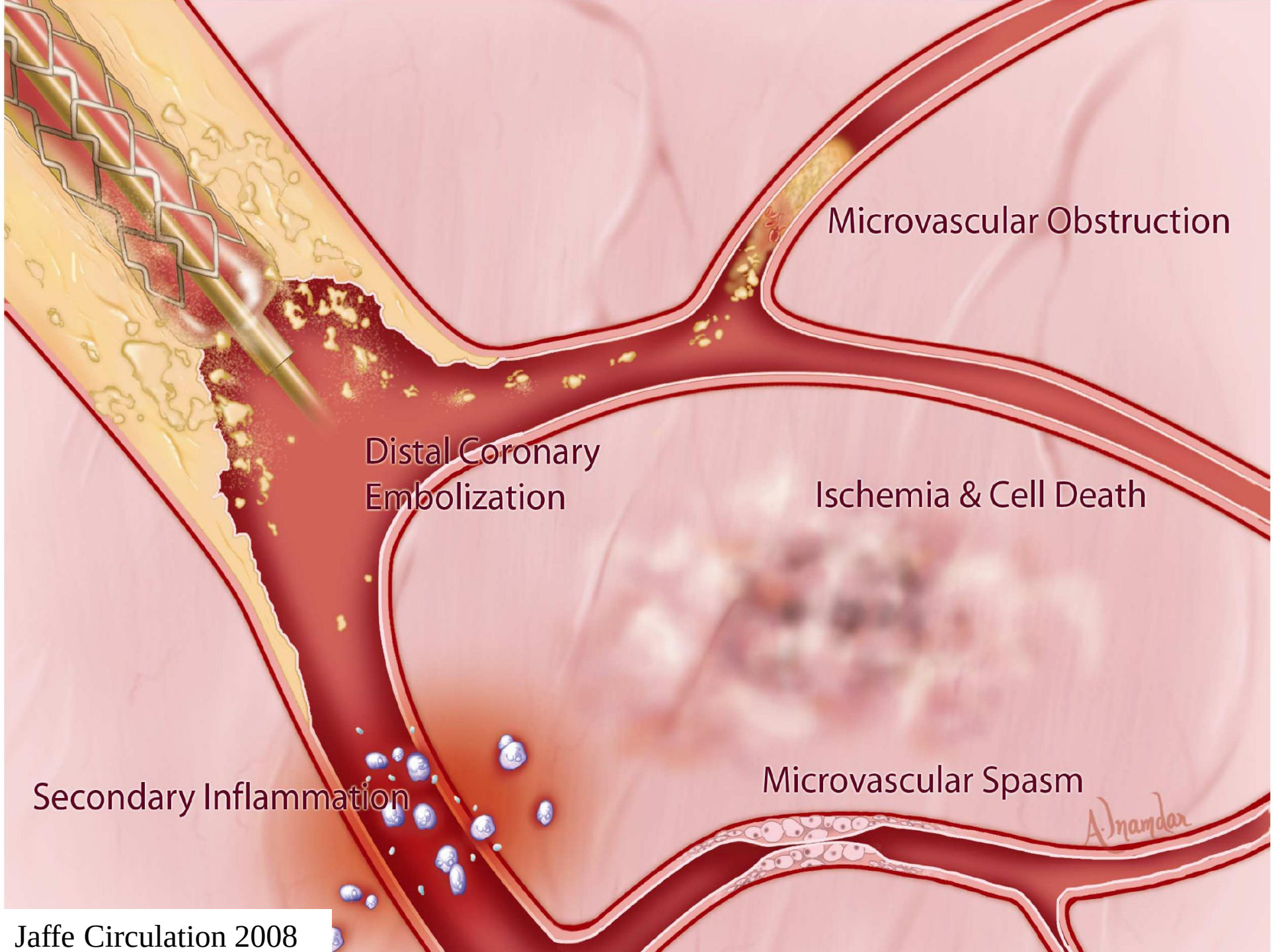
Microvascular obstruction following PCI

Clinical setting:



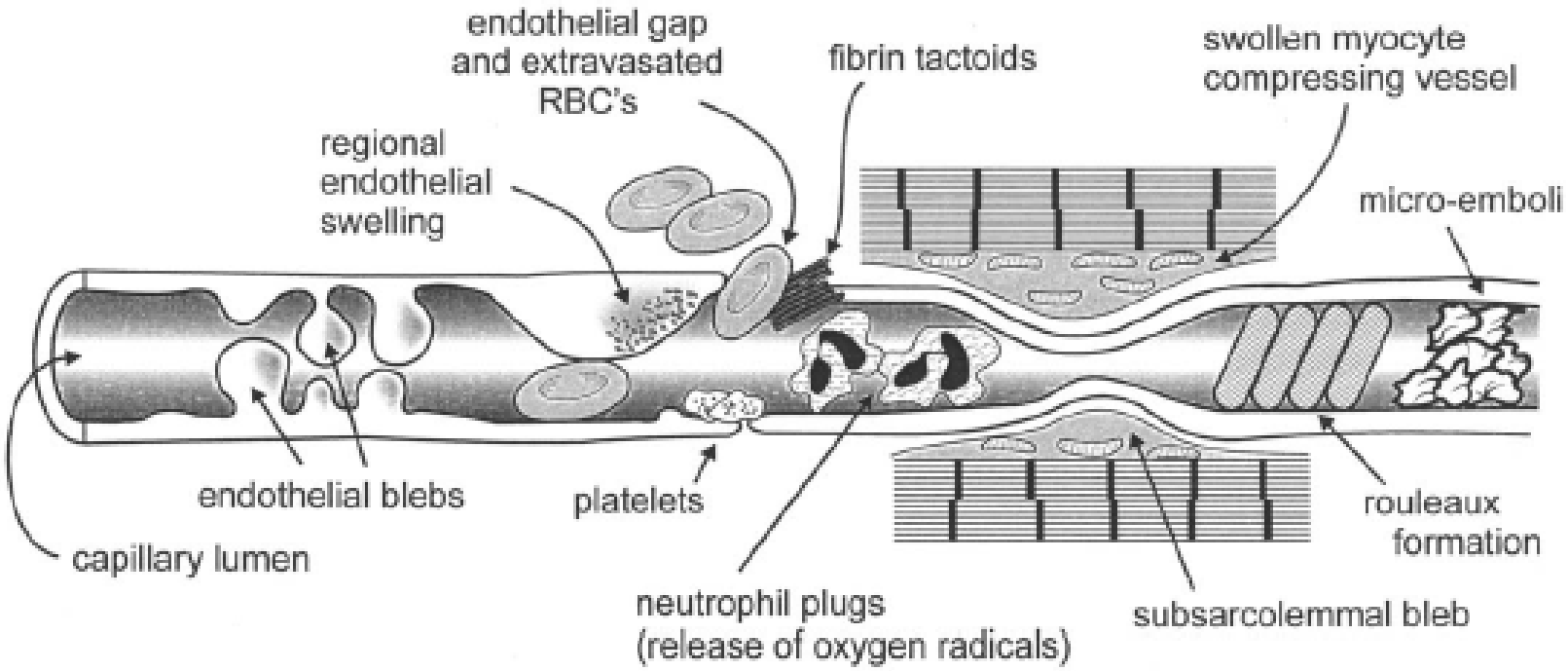
Pathophysiology of NR:





Jaffe Circulation 2008

Experimental Ischemia-reperfusion model



Microvascular obstruction is confined to the irreversibly damaged necrotic zone.

Kloner Circulation 1980;62:945-52.

Predictors of No-reflow:

Interventional NR:

- Degenerated SVG
- Thrombus containing lesions
- Atherectomy

Reperfusion NR (STEMI):

- Duration of ischemia
- Smoking
- Age
- Diabetes
- Hyperlipidemia
- Renal failure
- Thromotic lesion
- High-pressure inflation

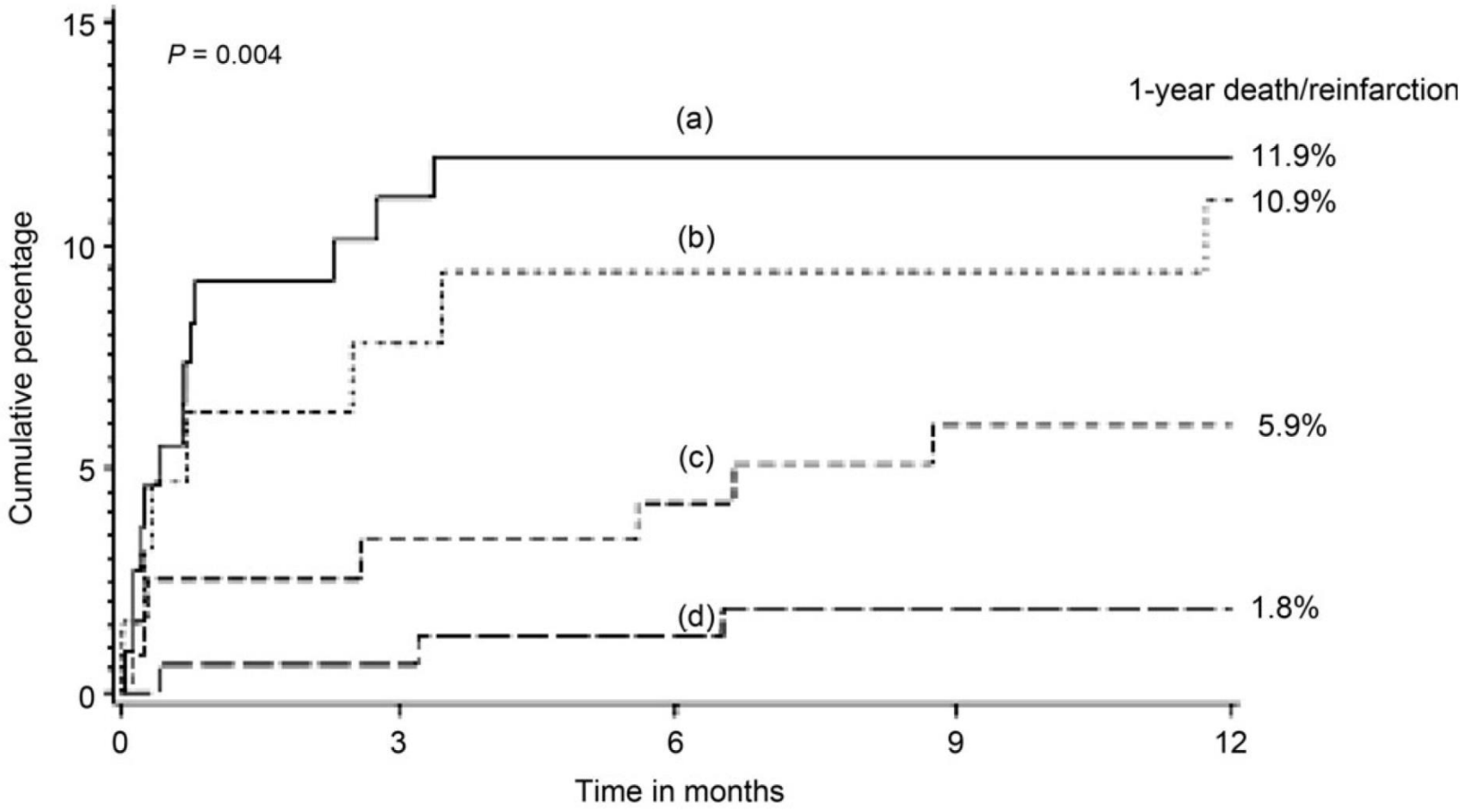
Diagnosis of microvascular obstruction:

- Chest pain
- ST-elevation
- No ST-segment resolution
- Elevated biomarkers ~ 70%
- Angiographic no-reflow
  - TIMI flow
  - TIMI frame count
  - Myocardial blush grade
- Contrast echo
- Contrast CT
- Contrast MRI

Clinical significance of NR:

- Increased infarct size
- Heart failure
- Arrhythmia
- Mortality

CADILLAC: ST-Σ & myocardial blush after PPCI



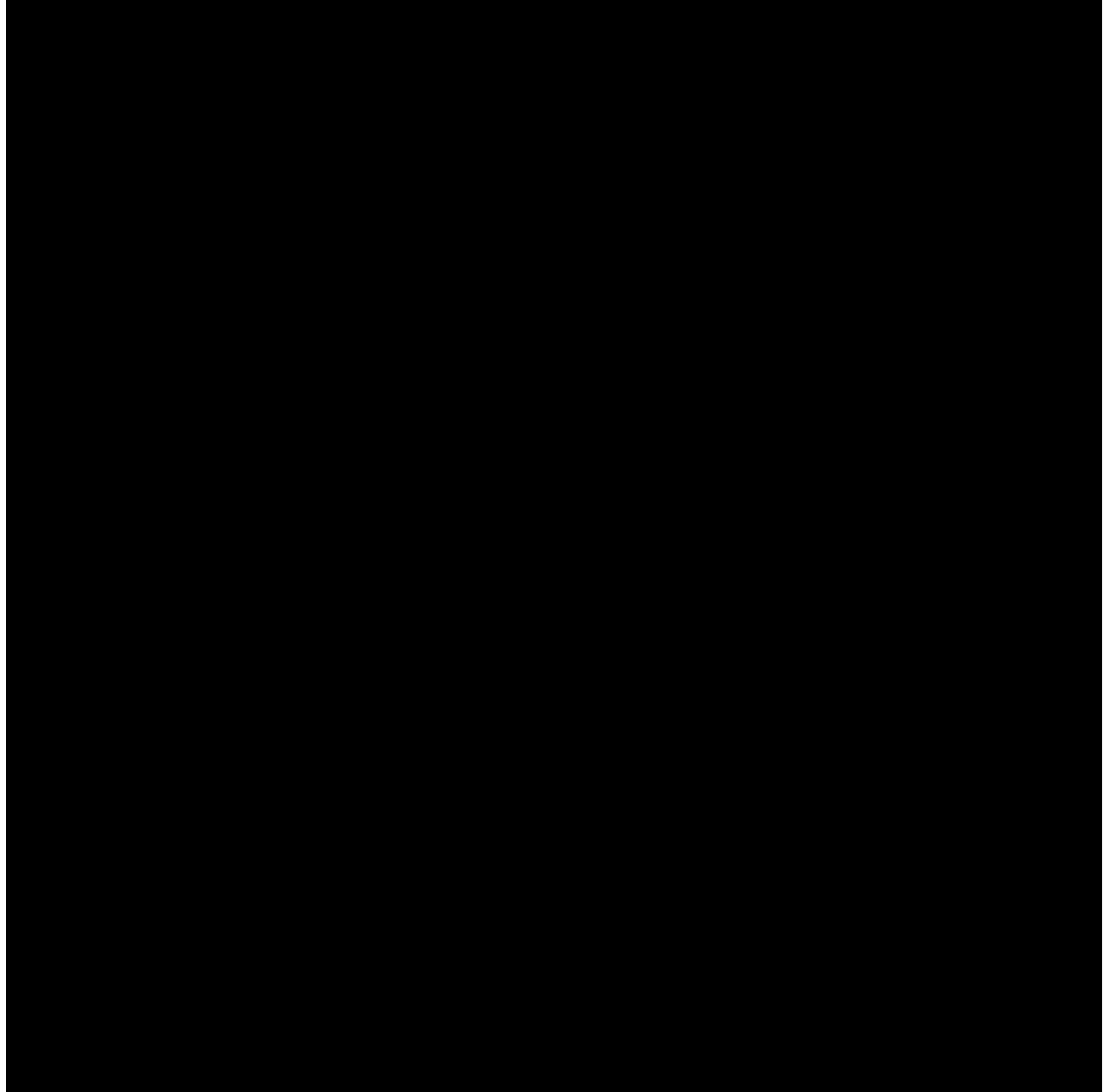
Number at risk					
Σ < 70%, Blush 0/1 (a)	109	96	95	95	95
Σ < 70%, Blush 2/3 (b)	54	59	58	58	57
Σ > 70%, Blush 0/1 (c)	118	114	113	111	111
Σ > 70%, Blush 2/3 (d)	165	161	158	156	156

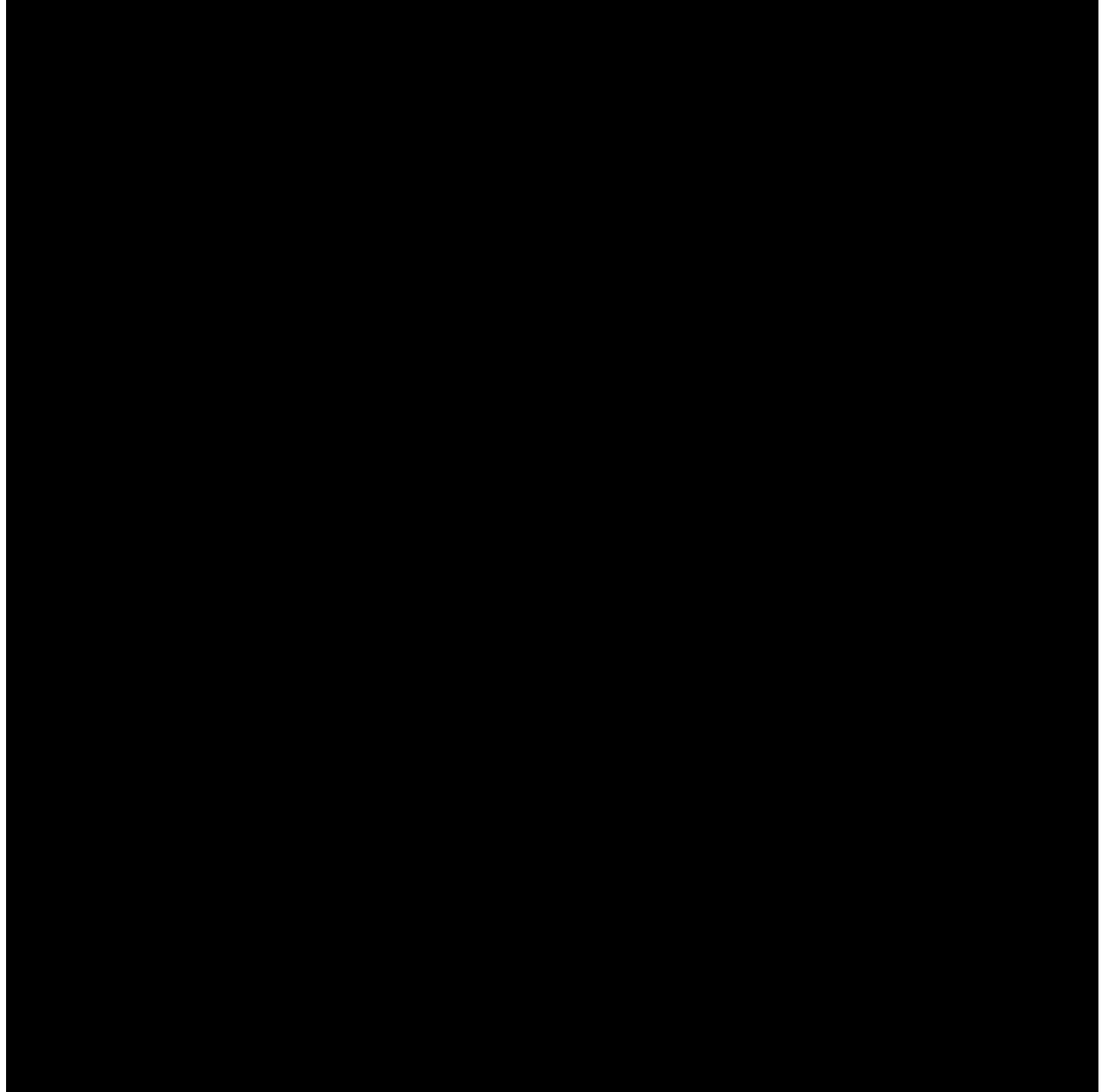
Sorajja Eur Heart J 2005;26:667–674

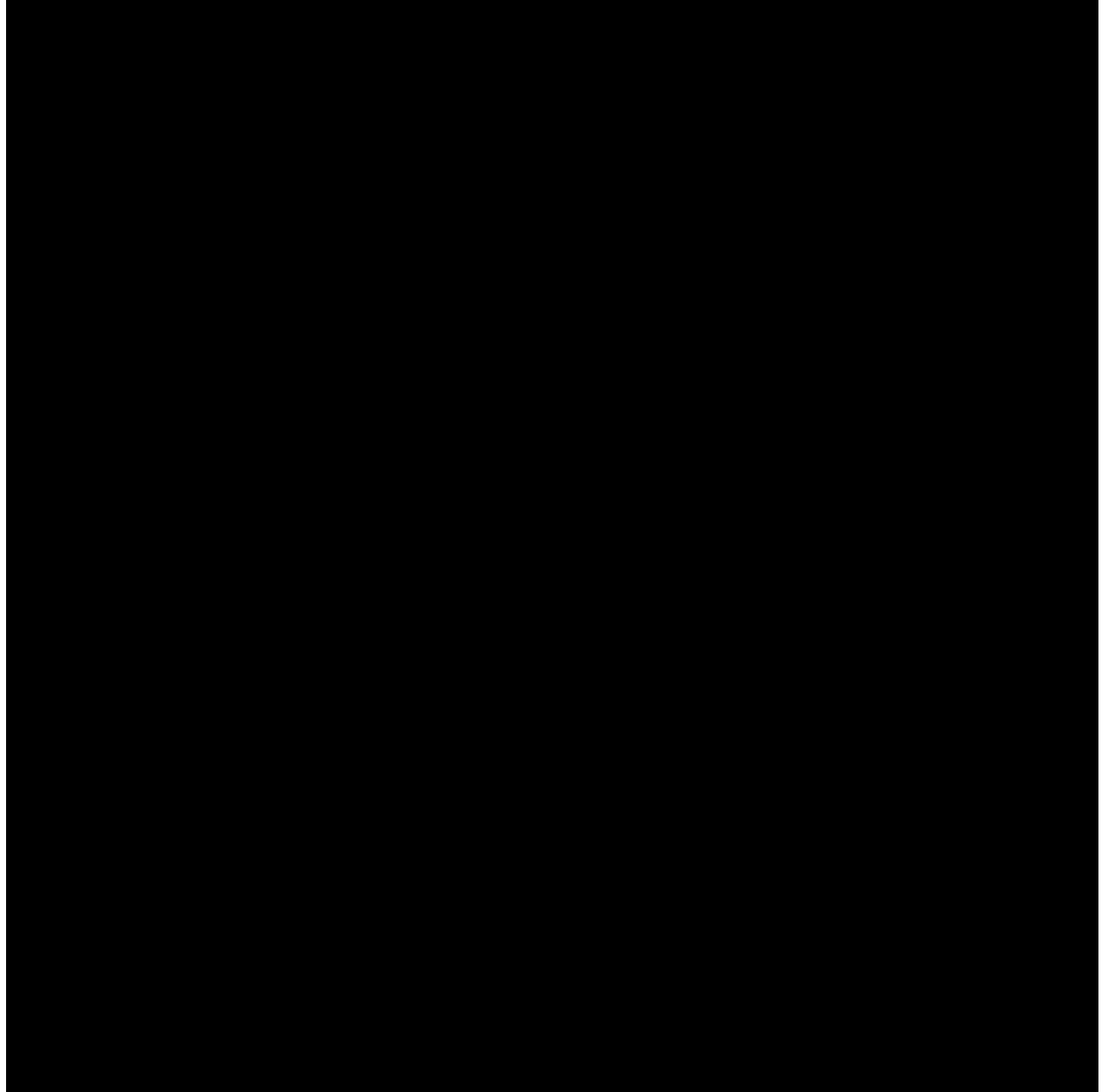
Case #1:

- 39 year-old male
- No known risk factors for ASCVD
- Anterior STEMI
- Symptom to balloon time=2 hours

- Primary PCI to proximal LAD
  - Thrombus aspiration
  - DES implantation





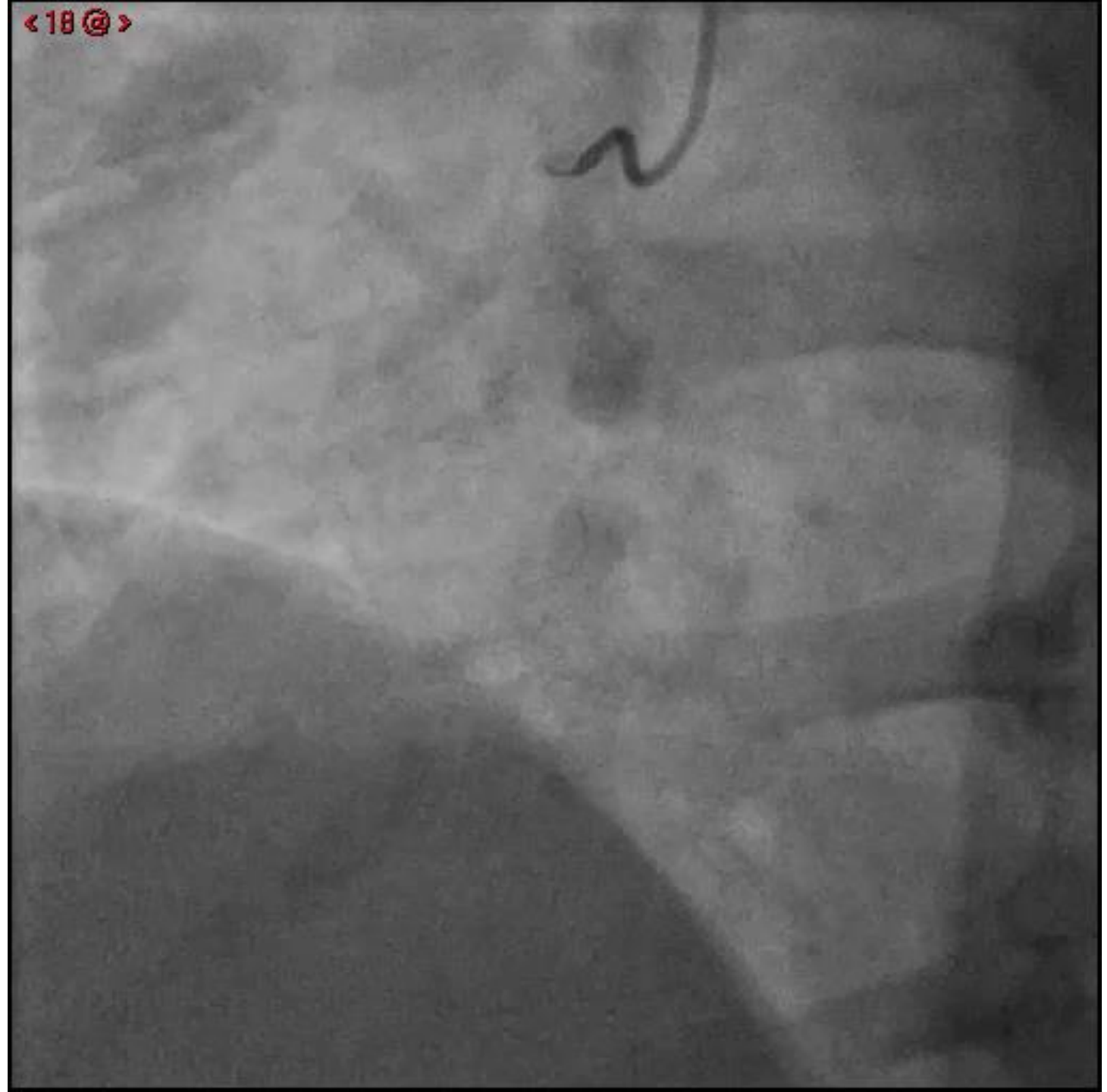


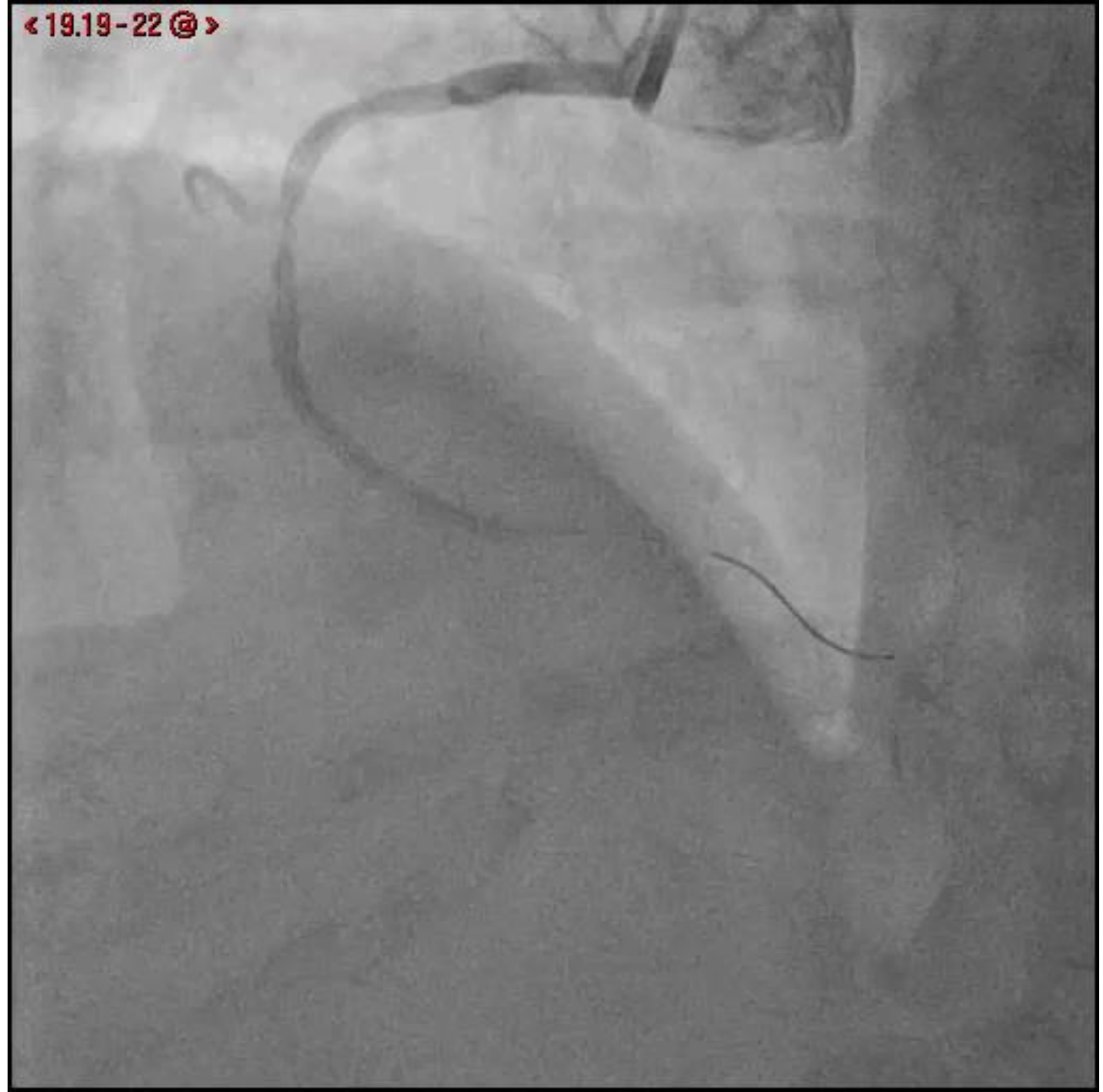
Procedural outcome:

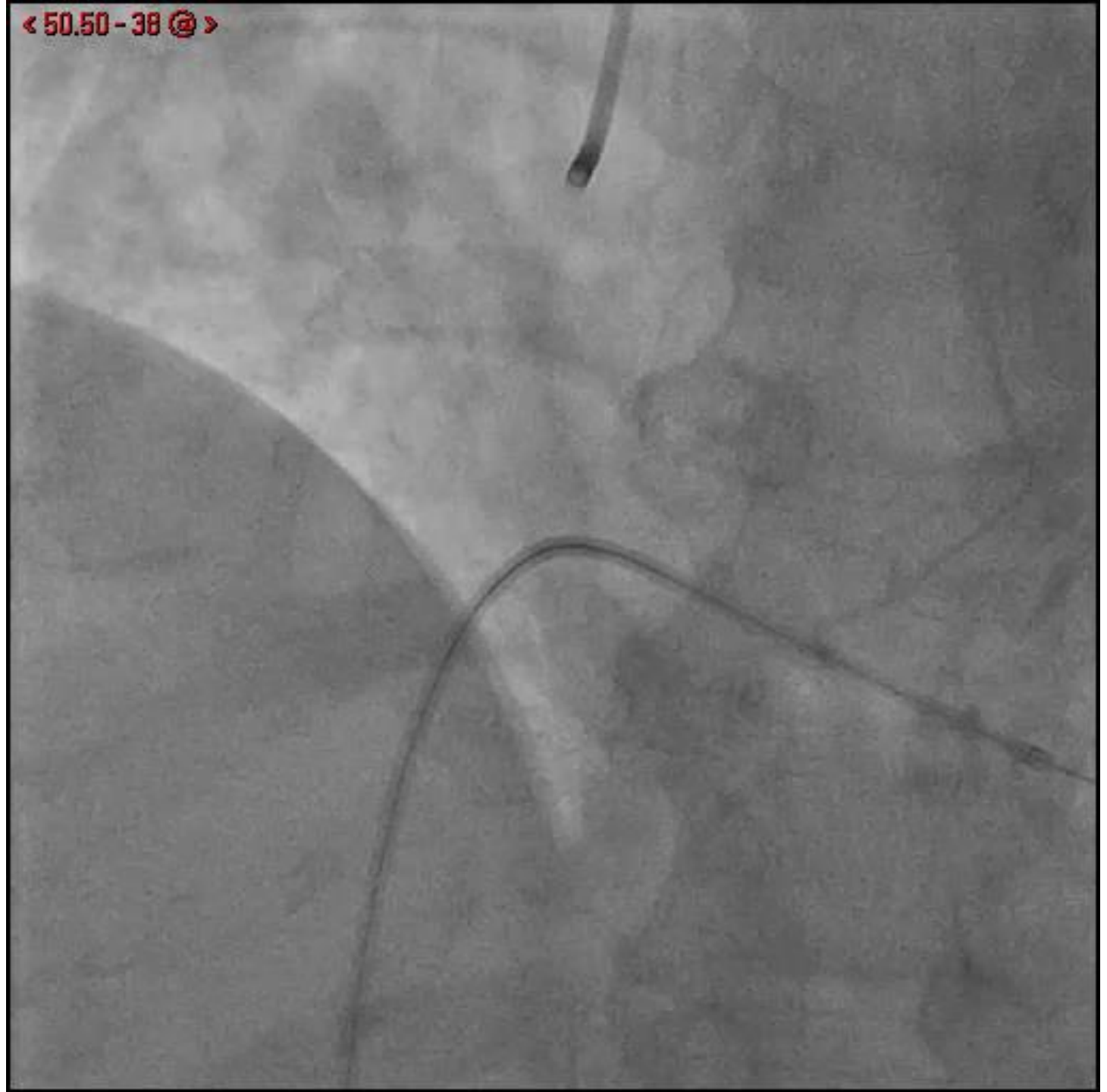
- No-reflow
- Ischemic cardiomyopathy, EF=15%
- Cardiac arrest-ACLS
- Anoxic brain damage
- LVAD
- Heart transplant

Case #2:

- 53 year-old female
- Diabetes mellitus, smoker, hypertension, hyperlipidemia
- 2018:
  - NSTEMI
  - Critical proximal & distal RCA lesions
  - PCI to RCA


‹ 18 @ ›


« 19.19 - 22 @ »

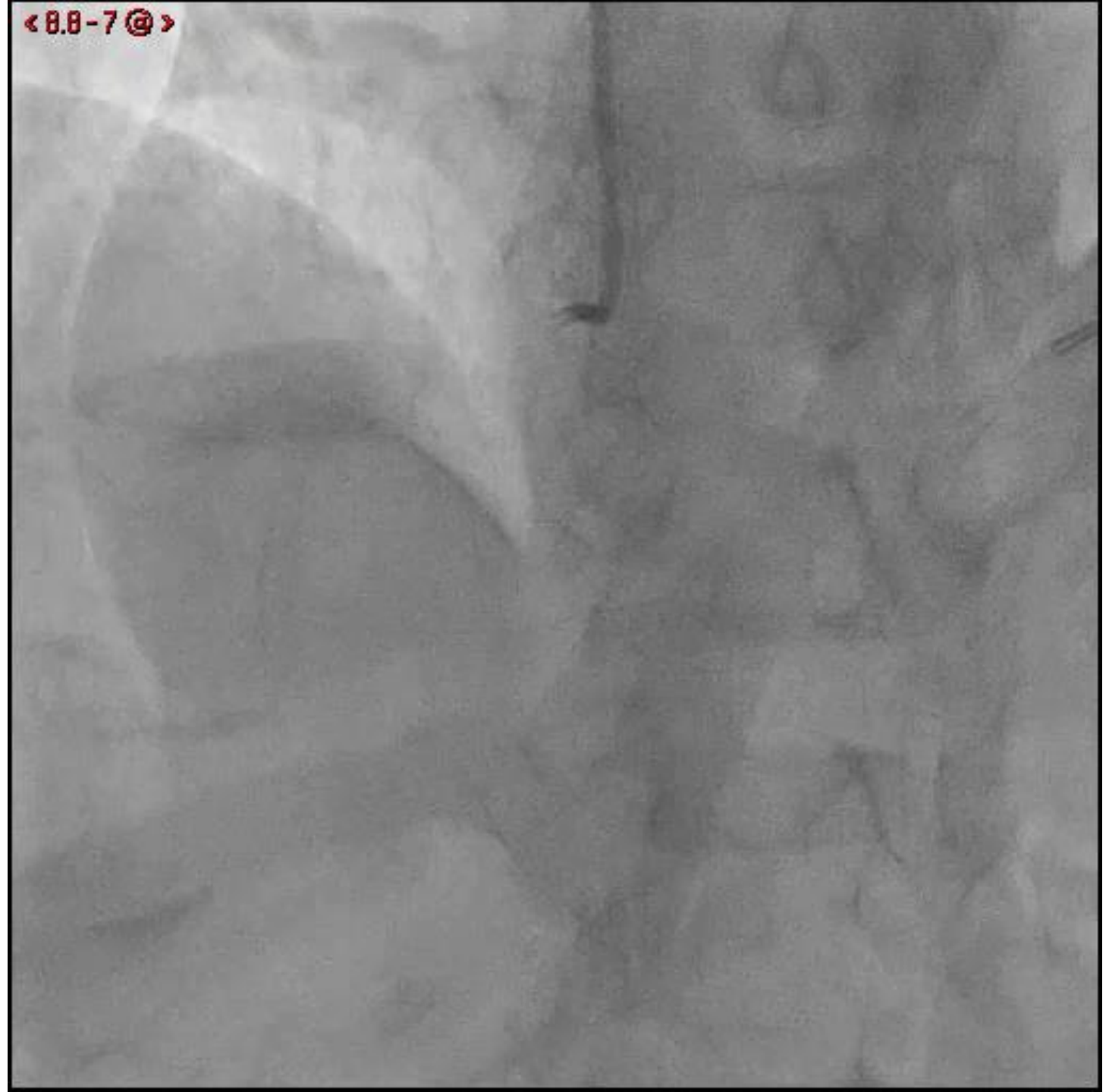

« 50.50 - 38 @ »

Procedural outcome:

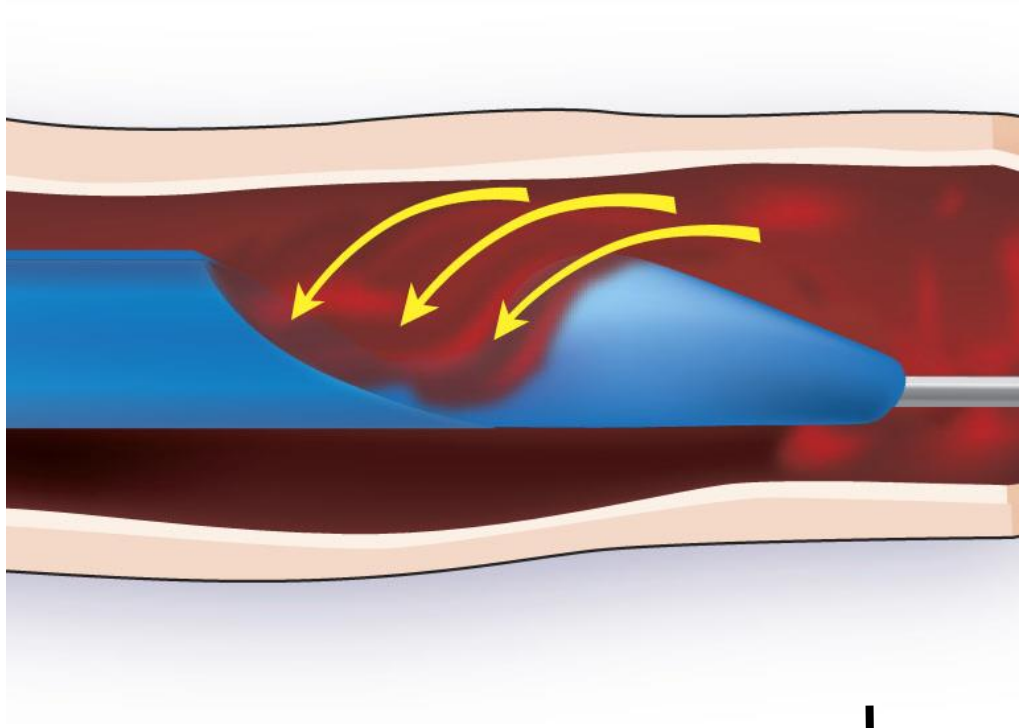
- No-reflow
- Asystole
- CPR + temporary pacemaker
- IC adenosine & integrilin

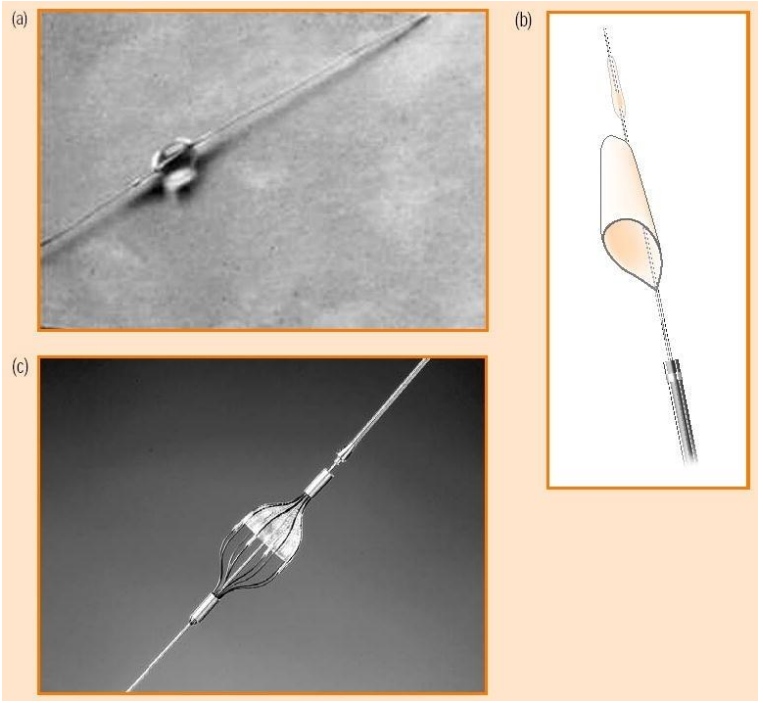
2022 (4 years later):

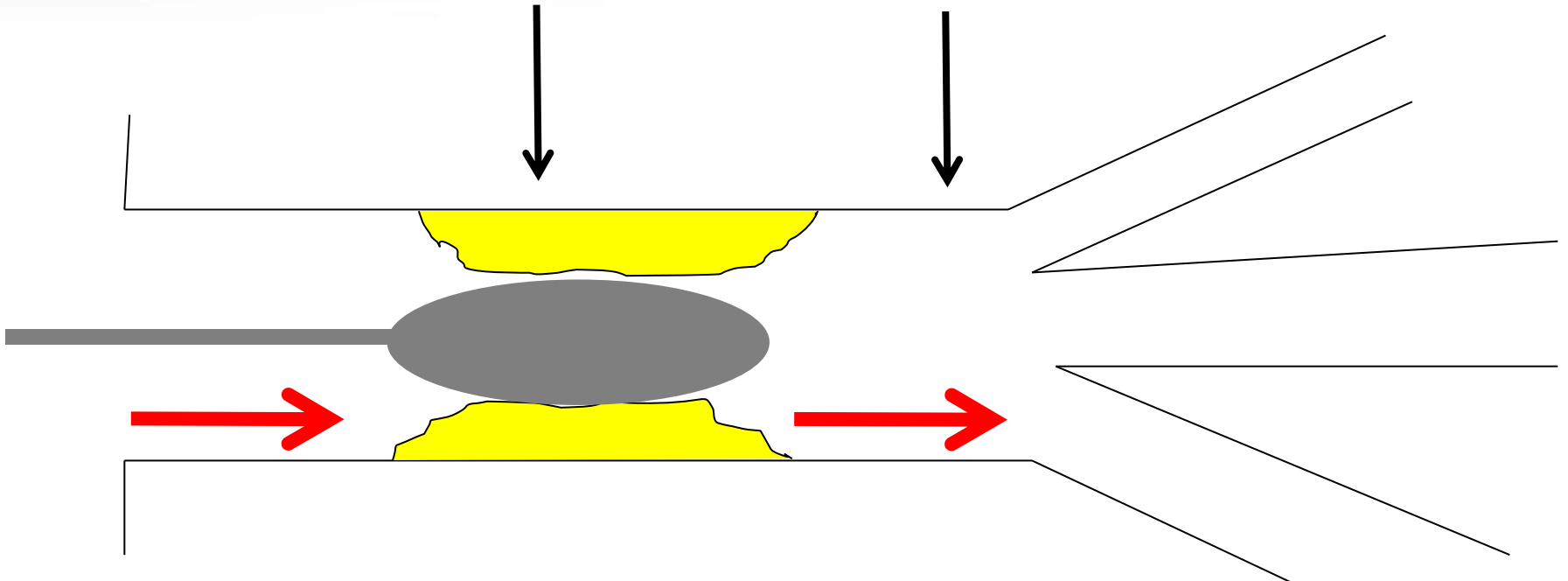
- Echo: normal LV function
- RCA: TIMI-3 flow


«8.8-7@»

Devices for preventing no reflow

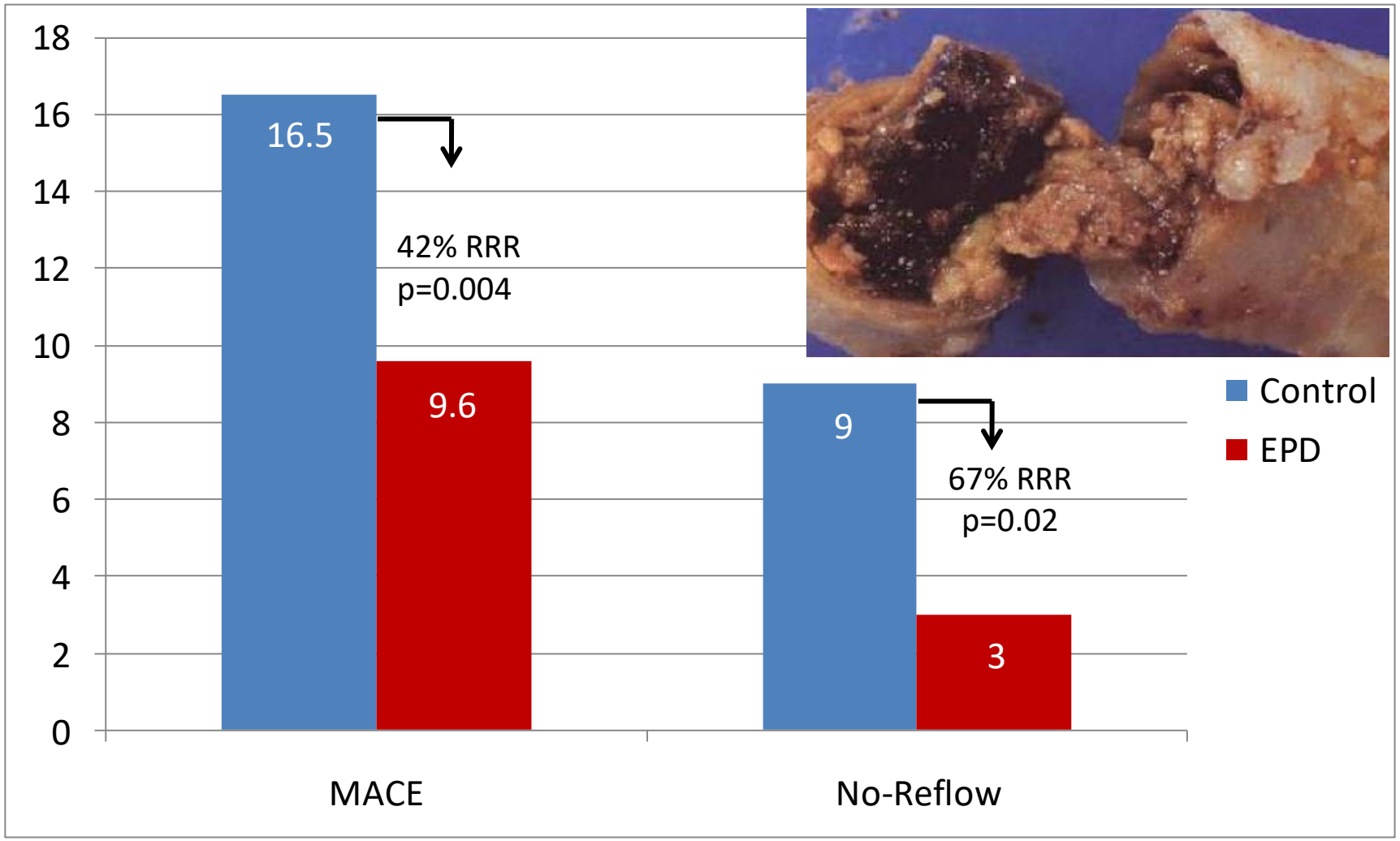



(a)
(b)
(c)



Embolic protection

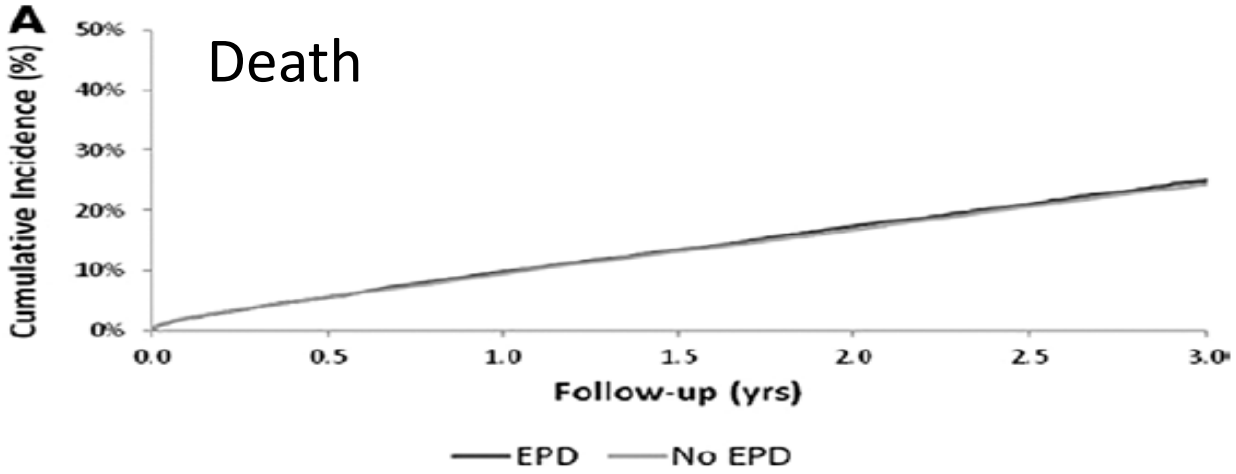
SAFER: RCT of embolic protection device during bypass graft PCI (801 pts)

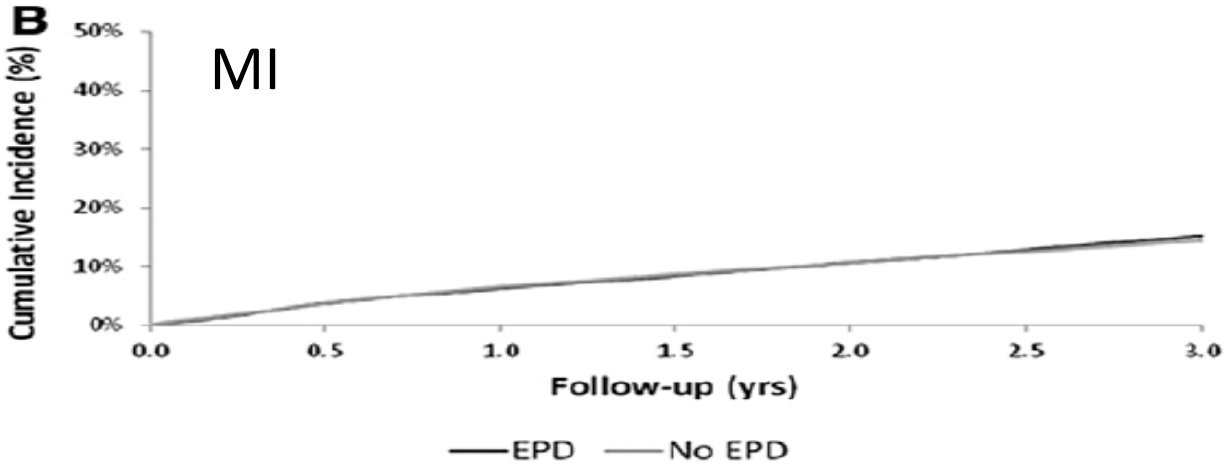


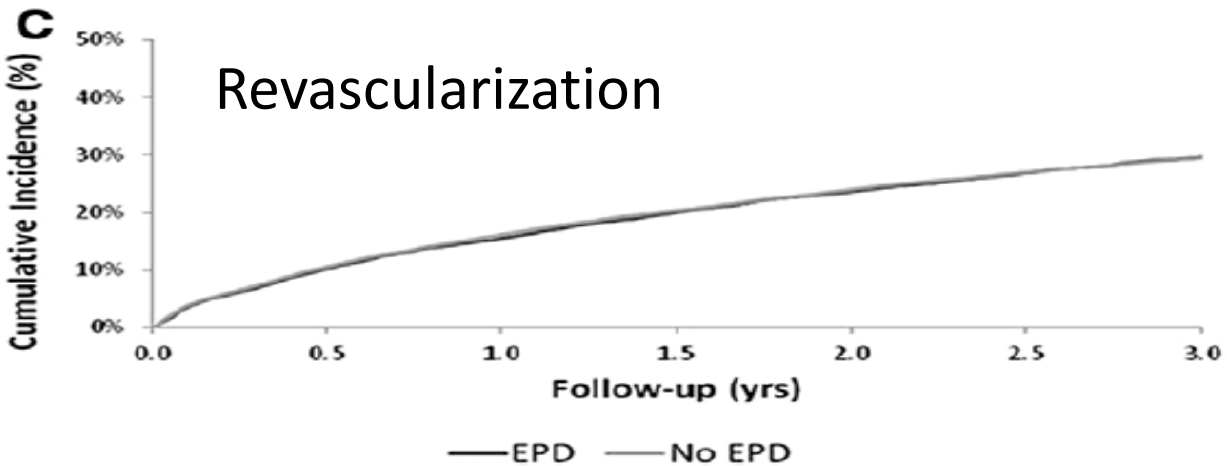
AHA/ACC 2011 guidelines: Class 1 indication

ESC 2010 guidelines: Class 1 indication

Baim Circulation 2002;105:1285







NCDR CathPCI registry

-49,325 patients undergoing SVG PCI

-EPD (n=10,432) No EPD (n=38,893)

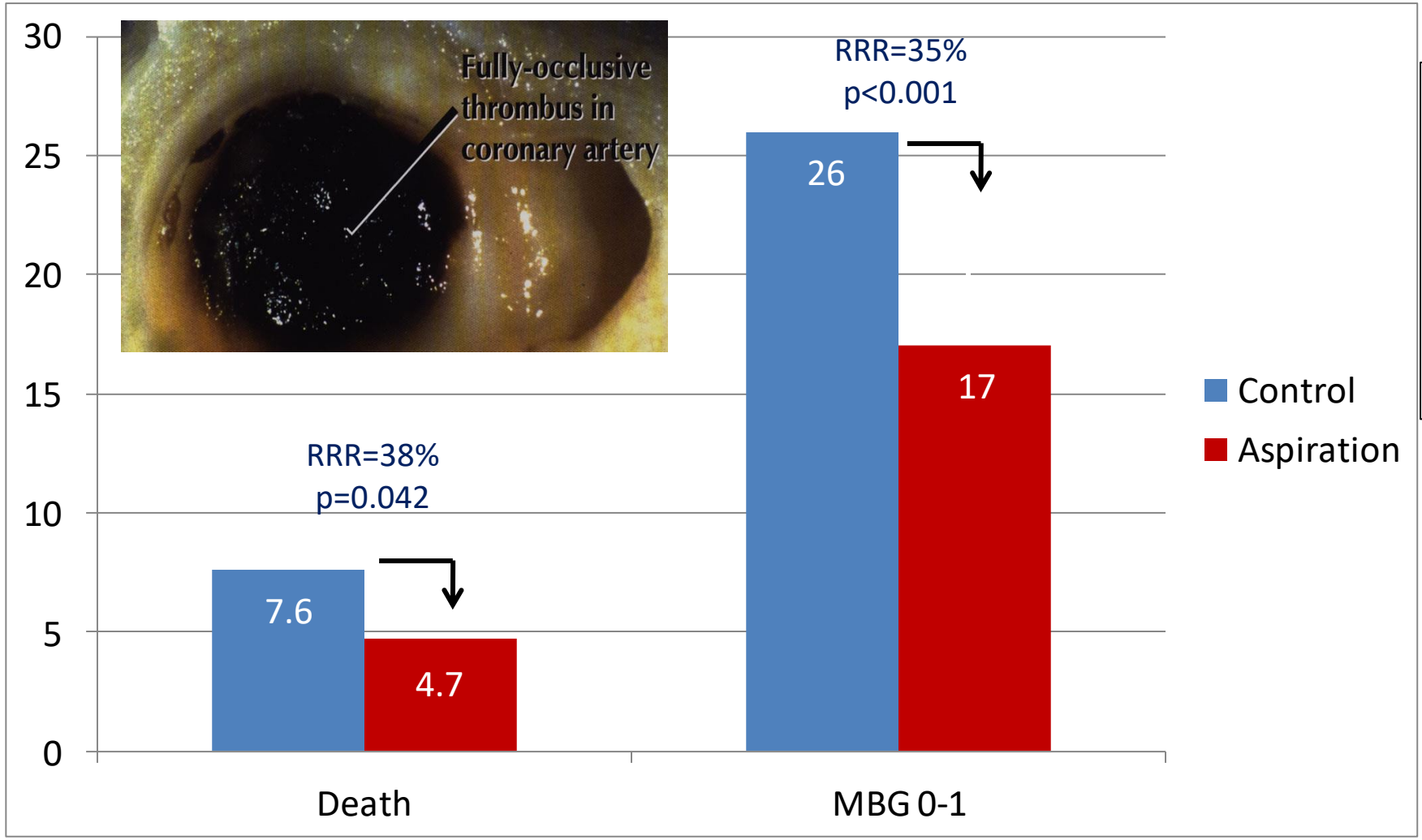
AHA/ACC 2022 guidelines: Class 2a indication

ESC 2018 guidelines: ??

Brennan *Circ Cardiovasc Interv*. 2015

Thrombus aspiration

TAPAS: Randomized trial of thrombus aspiration during AMI PCI (1,071 pts)

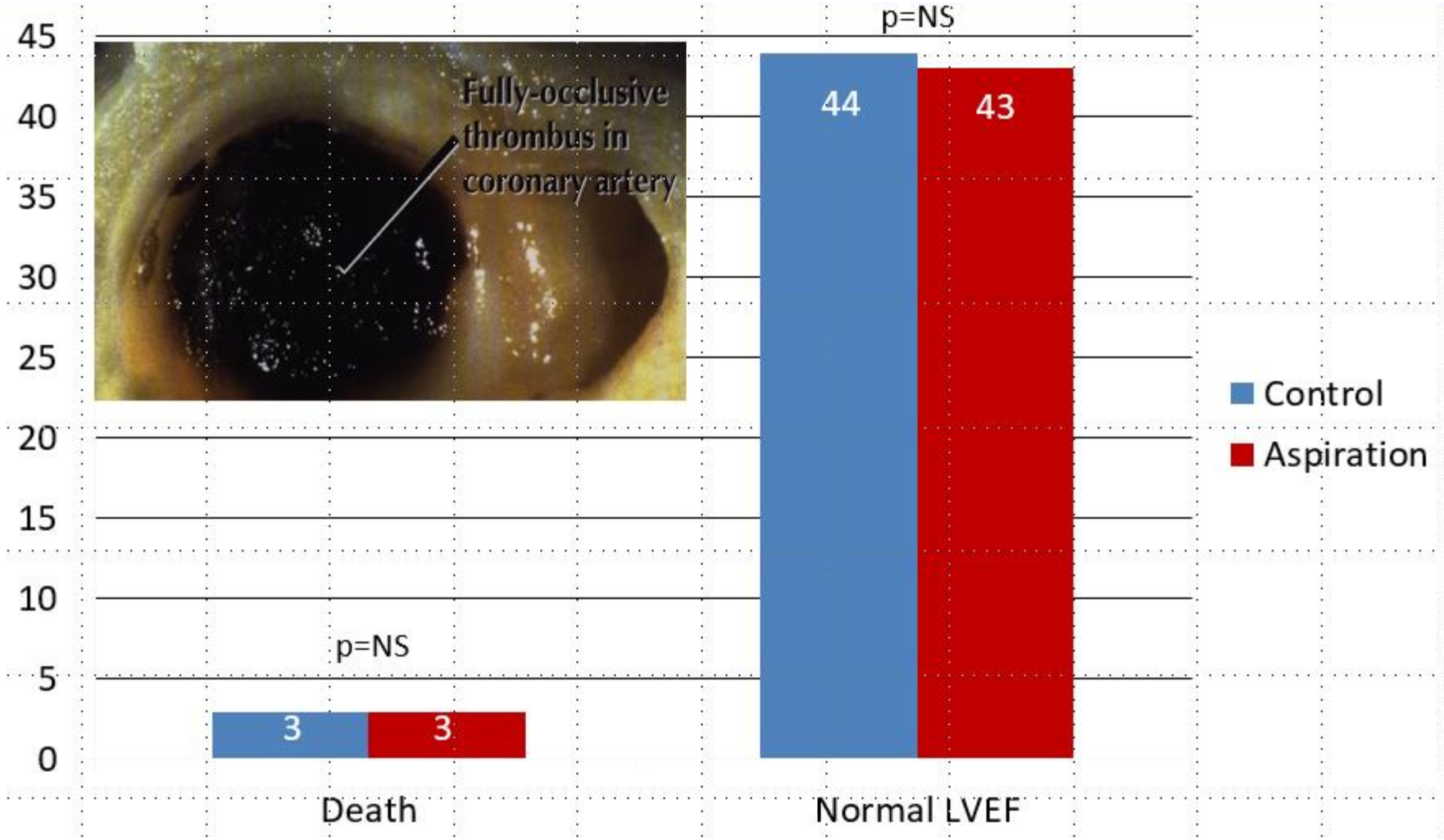


AHA/ACC 2011 guidelines: Class 2a indication

ESC 2010 guidelines: Class 2a indication

Vlaar Lancet 2008;371:1915

TASTE: Randomized trial of thrombus aspiration during AMI PCI (7,244 pts)



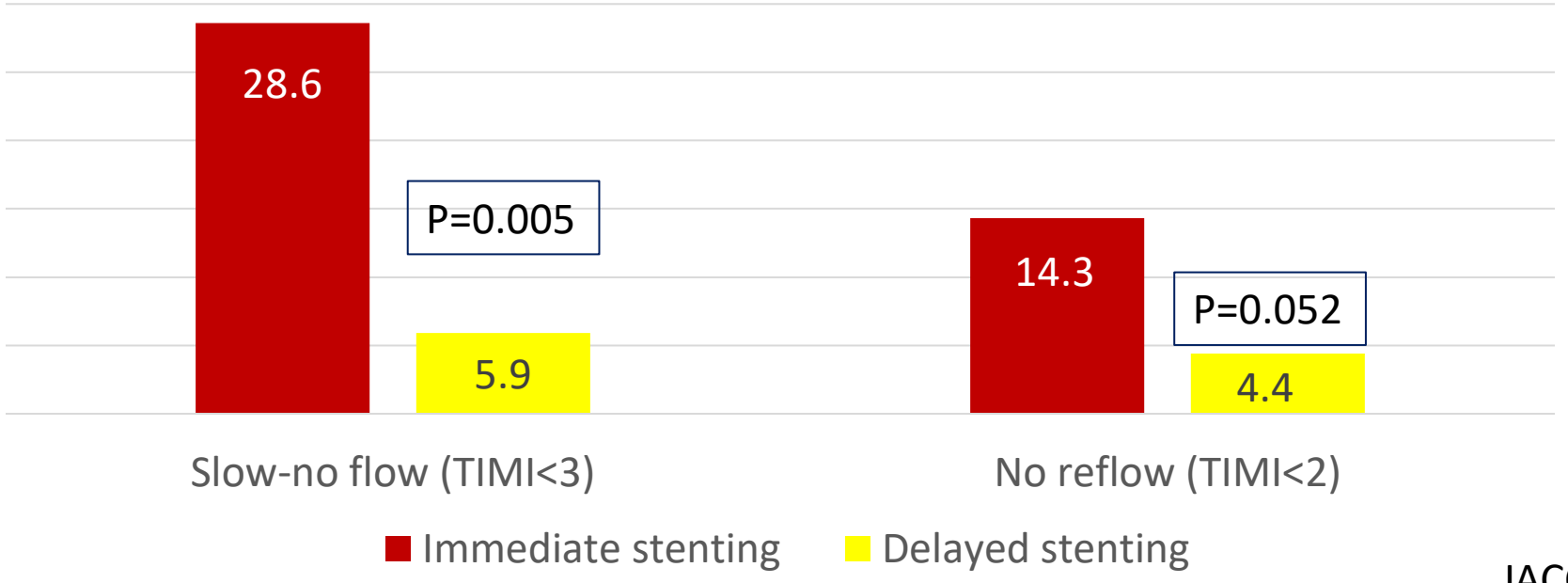
AHA/ACC 2022 guidelines: Class 3 indication

ESC 2018 guidelines: Class 3 indication

Fröbert NEJM 2013;371:1915

A Randomized Trial of Deferred Stenting Versus Immediate Stenting to Prevent No- or Slow-Reflow in Acute ST-Segment Elevation Myocardial Infarction (DEFER-STEMI)

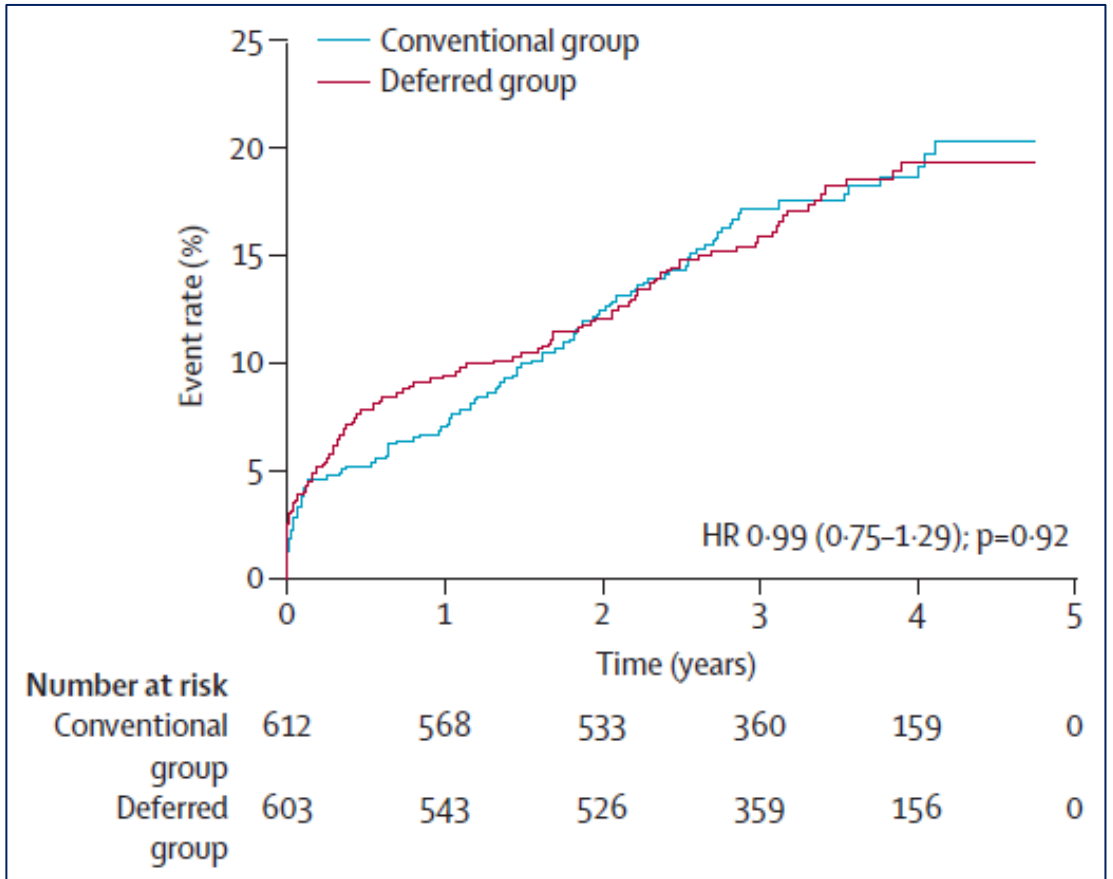
- 101 STEMI patients randomized to immediate vs. deferred stenting



JACC 2014 2014:2088–98

Deferred versus conventional stent implantation in patients with ST-segment elevation myocardial infarction (DANAMI 3-DEFER): an open-label, randomised controlled trial

- 1215 STEMI patients randomized to immediate vs. deferred stenting
- Endpoint: Death, CHF, recurrent MI,revascularization
- TIMI-3 flow=96% in both groups



Lancet 2016; 387: 2199–206

Drugs for preventing and treating no reflow

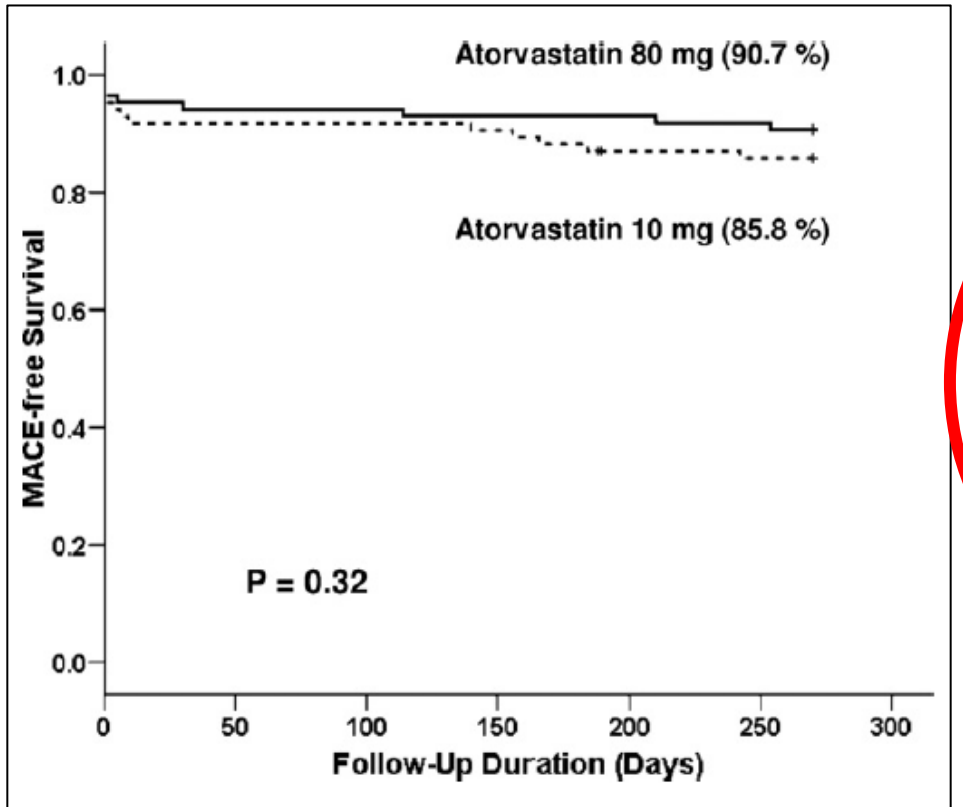
- Pre-clinical (animal) studies did not translate into clinical success
- Several studies of prophylactic pharmacotherapy
- No randomized trials of reversal of existing no reflow

- Vasodilators:
  - Adenosine
  - Ca blockers: verapamil, diltiazem
  - Nitroprusside
- Epinephrine
- Glycoprotein IIbIIIa inhibitors
- Statins
- IC fibrinolysis

Efficacy of High-Dose Atorvastatin Loading Before Primary Percutaneous Coronary Intervention in ST-Segment Elevation Myocardial Infarction

The STATIN STEMI Trial

- 171 STEMI patients randomized to 80 or 10 mg atorvastatin before PPCI

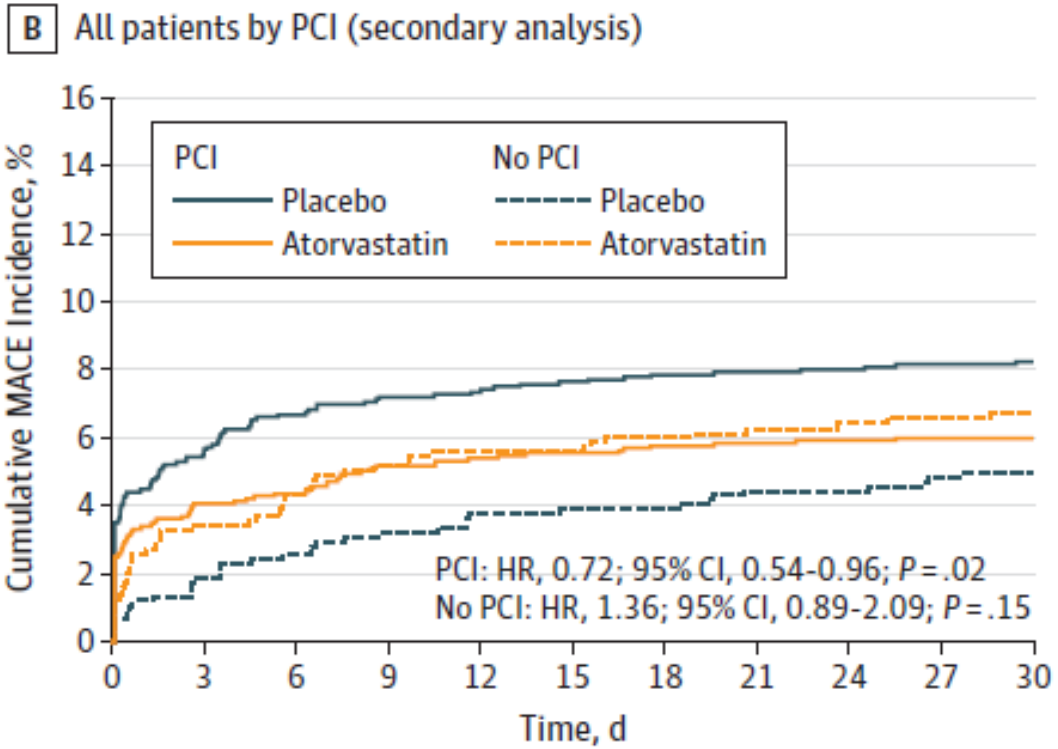


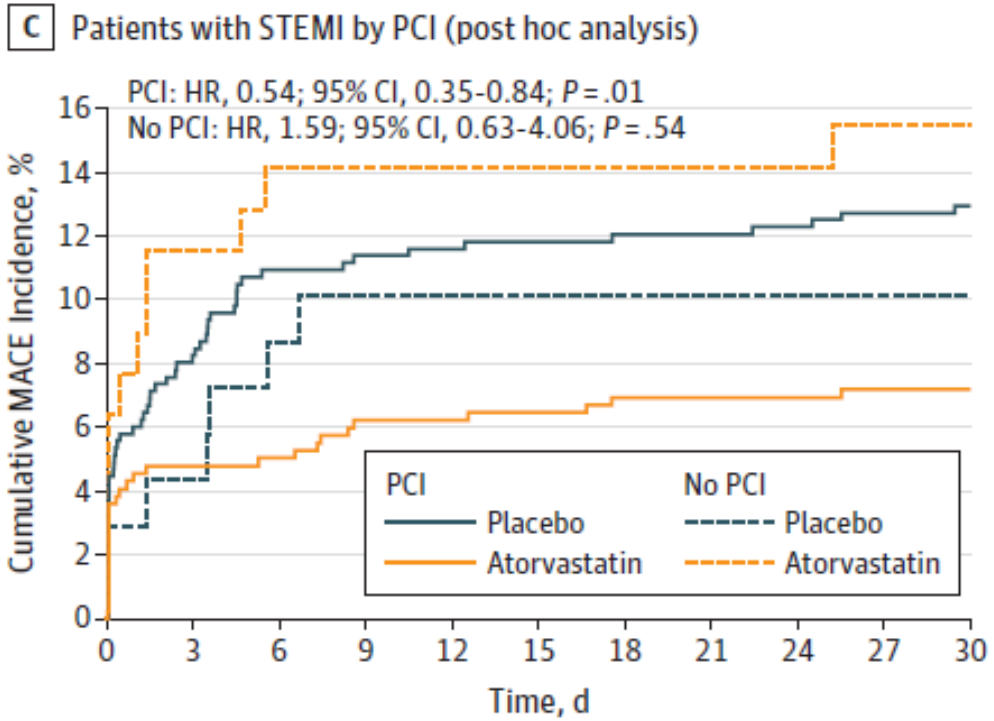
	Atorvastatin		
	80 mg (n = 86)	10 mg (n = 85)	p Value
TIMI blush grade	2.2 ± 0.8	1.9 ± 0.8	0.02
Corrected TIMI frame count	26.9 ± 12.3	34.1 ± 19.0	0.01
Mean ST-segment resolution	61.8 ± 26.2	50.6 ± 25.8	0.01
Complete ST-segment resolution	34 (39.5)	19 (23.8)	0.03

JACC Cardiovasc. Interv. **2010**, 3, 332–339.

Effect of Loading Dose of Atorvastatin Prior to Planned Percutaneous Coronary Intervention on Major Adverse Cardiovascular Events in Acute Coronary Syndrome
The SECURE-PCI Randomized Clinical Trial

- 4191 ACS patients randomized to 80 mg atorvastatin vs placebo before catheterization



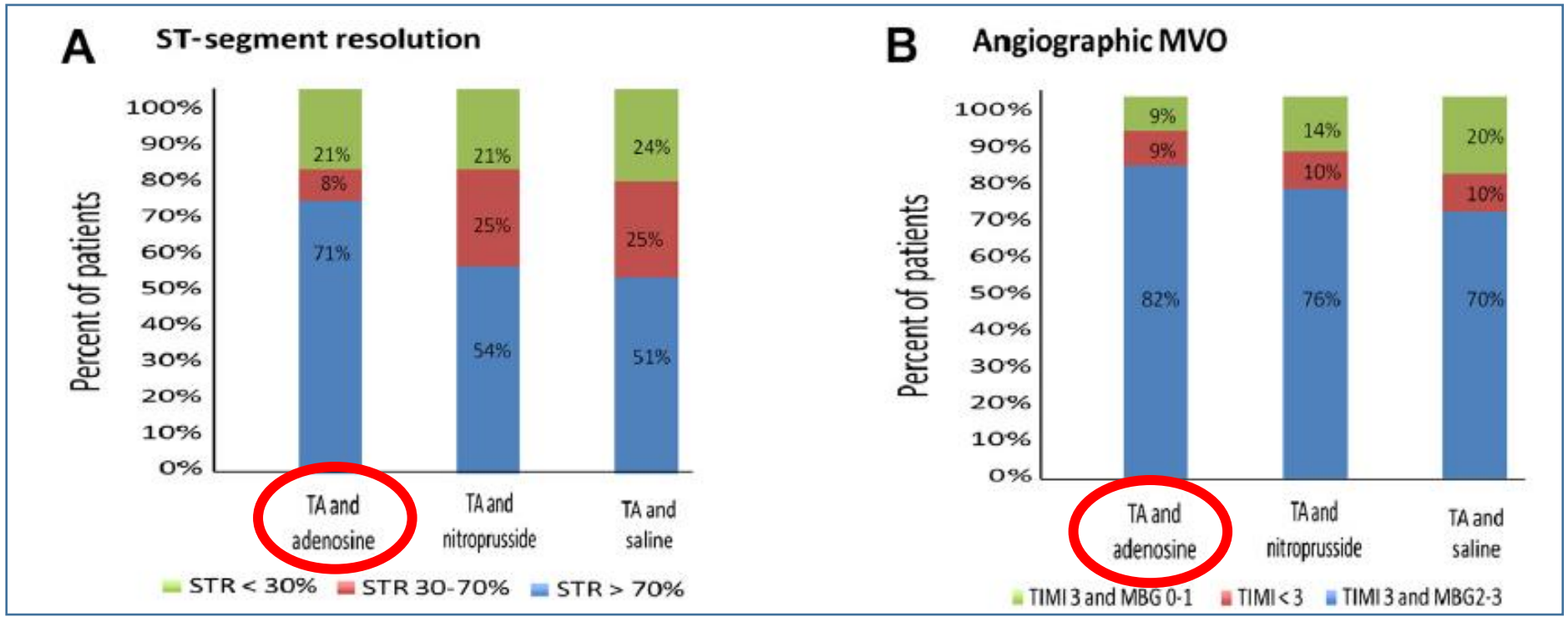


JAMA. 2018; 319(13): 1331-1340

Open-Label, Randomized, Placebo-Controlled Evaluation of Intracoronary Adenosine or Nitroprusside After Thrombus Aspiration During Primary Percutaneous Coronary Intervention for the Prevention of Microvascular Obstruction in Acute Myocardial Infarction

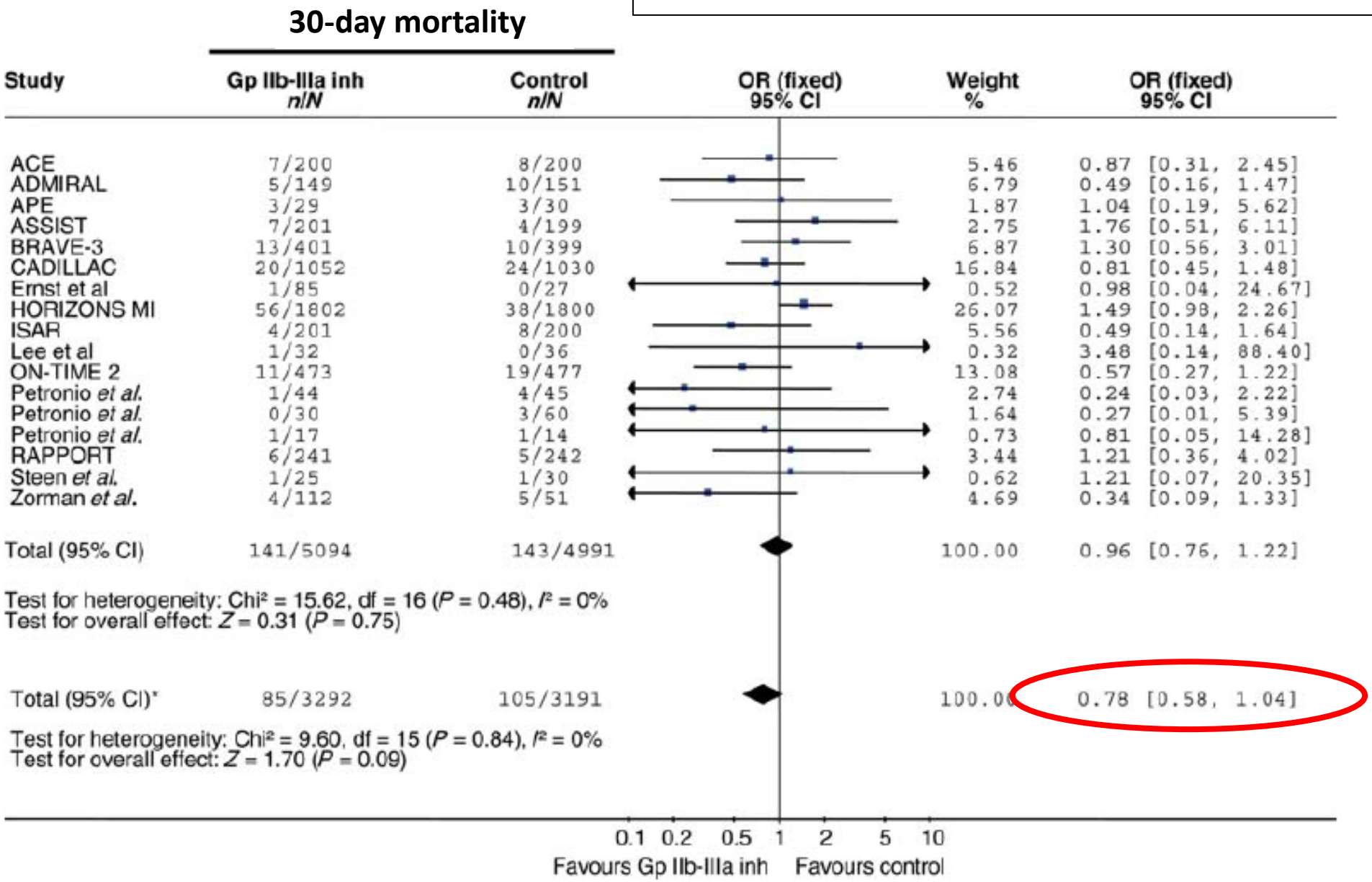
The REOPEN-AMI Study (Intracoronary Nitroprusside Versus Adenosine in Acute Myocardial Infarction)

- 240 STEMI patients randomized to adenosine / nitroprusside / saline



JACC Intv 2013; 6:580–9

GP2b3a inhibitors in STEMI



Eur Heart J 2009;30:2705–2713

Intracoronary Abciximab and Aspiration Thrombectomy in Patients With Large Anterior Myocardial Infarction

The INFUSE-AMI Randomized Trial

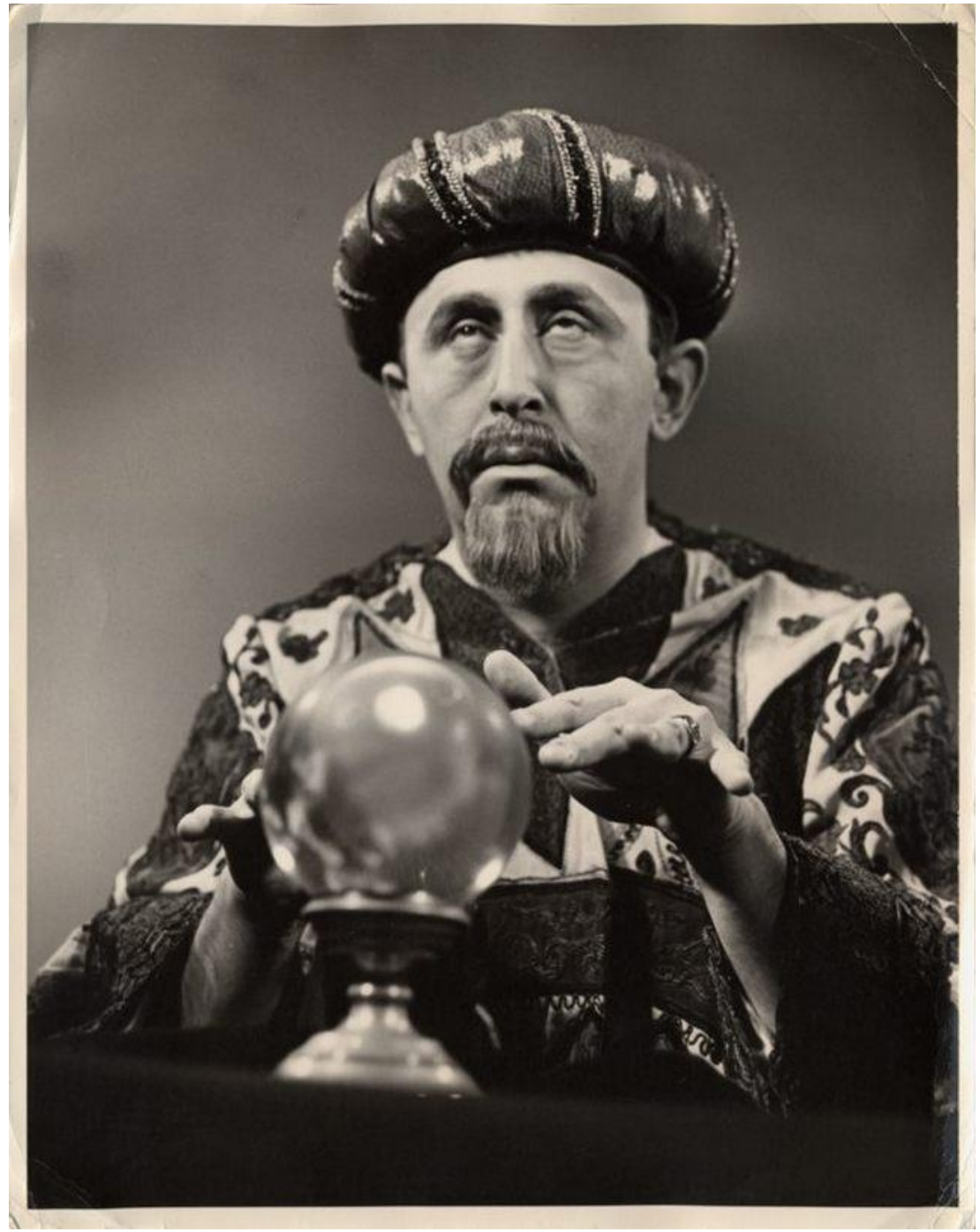
- 452 STEMI patients randomized (2X2). Endpoint=infarct size
  - IC abciximab vs none,
  - thrombectomy vs none

Table 3. Thirty-Day Cardiac Magnetic Resonance Imaging Results for the Pooled Randomized Groups

	Intracoronary Abciximab[a] (n = 188)	No Intracoronary Abciximab[a] (n = 184)	*P* Value	Aspiration Thrombectomy[b] (n = 186)	No Aspiration Thrombectomy[b] (n = 186)	*P* Value
Infarct size, median [IQR], % of total LV mass[c]	15.1 [6.8-22.7] (n = 181)	17.9 [10.3-25.4] (n = 172)	.03	17.0 [9.0-22.8] (n = 174)	17.3 [7.1-25.5] (n = 179)	.51
Total LV myocardial mass, median [IQR], g	128.6 [106.6-152.4] (n = 181)	130.4 [109.9-155.9] (n = 172)	.55	128.3 [108.9-149.8] (n = 174)	132.0 [107.6-156.1] (n = 179)	.50
Infarct mass, median [IQR], g	18.7 [7.4-31.3] (n = 184)	24.0 [12.1-34.2] (n = 175)	.03	20.3 [9.7-31.7] (n = 178)	21.0 [9.1-34.1] (n = 181)	.36

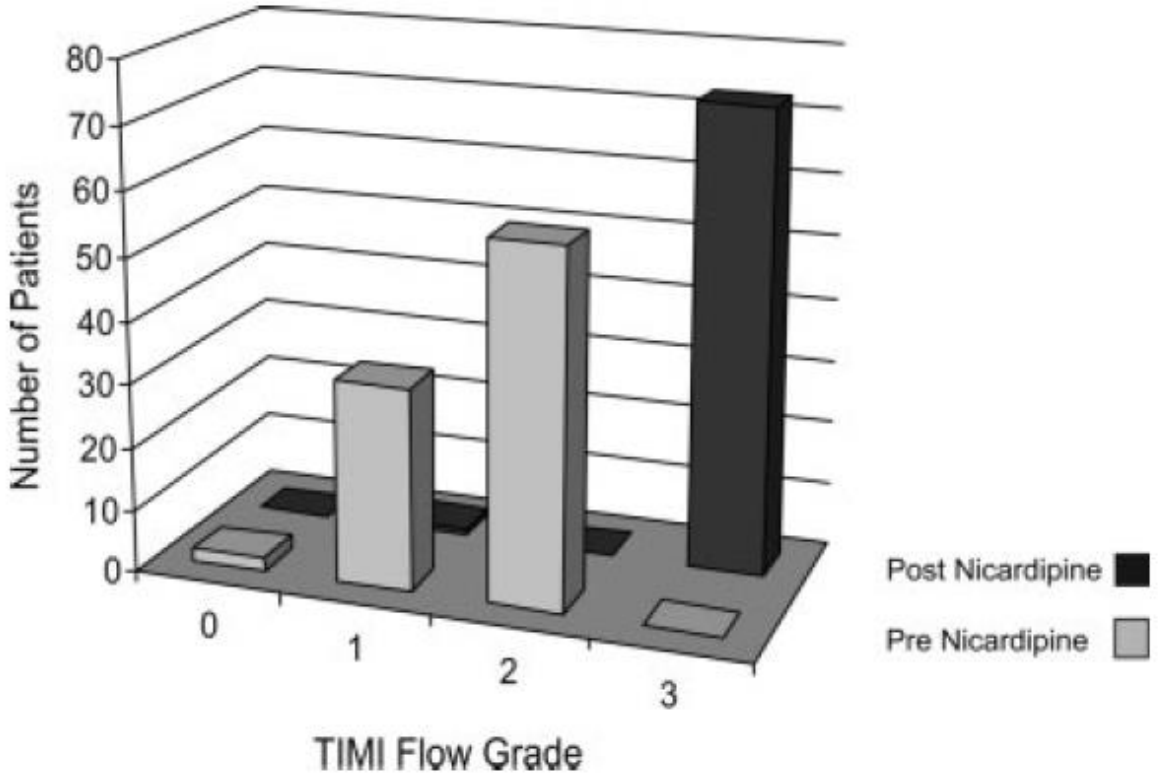
JAMA. 2012;307(17):1817-1826

Reversal of no reflow



Efficacy of Intracoronary Nicardipine in the Treatment of No-Reflow During Percutaneous Coronary Intervention

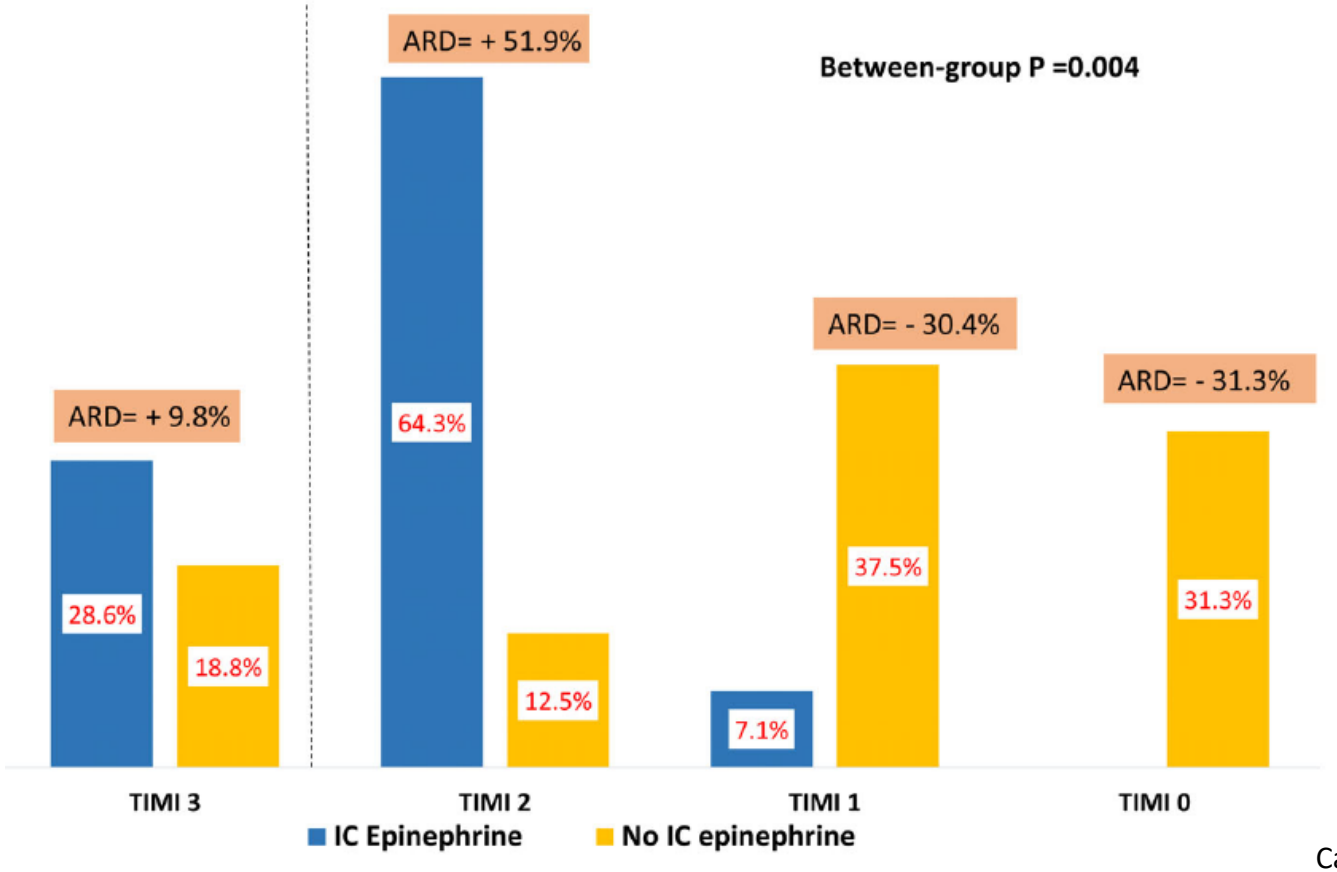
- Retrospective analysis of 72 patients who received IC nicardipine to reverse no-reflow



Cath Cardiovasc Interv 2006; 68:671–676

Efficacy and safety of intracoronary epinephrine versus conventional treatments alone in STEMI patients with refractory coronary no-reflow during primary PCI: The RESTORE observational study

- 30 consecutive patients with severe refractory no-reflow during PPCI



Catheter Cardiovasc Interv 2021;97:602–611


KEEP
CALM
BECAUSE
I DON'T
KNOW

LDCMC protocol-patients undergoing PCI:

- General:
  - High-dose statin
  - Treatment of hyperglycemia
- Prevention of interventional no-reflow:
  - SVG intervention: Distal embolic protection
  - Rota: Careful technique: short runs, maintain rota speed…
- Prevention of reperfusion no-reflow:
  - Adequate anticoagulation/ GP2b3a??
  - Achieve TIMI-3 flow before stenting
  - Avoid high inflation pressures
- Reversal of NR:
  - IC Adenosine

Thank you

TAPAS

2008

The NEW ENGLAND JOURNAL of MEDICINE

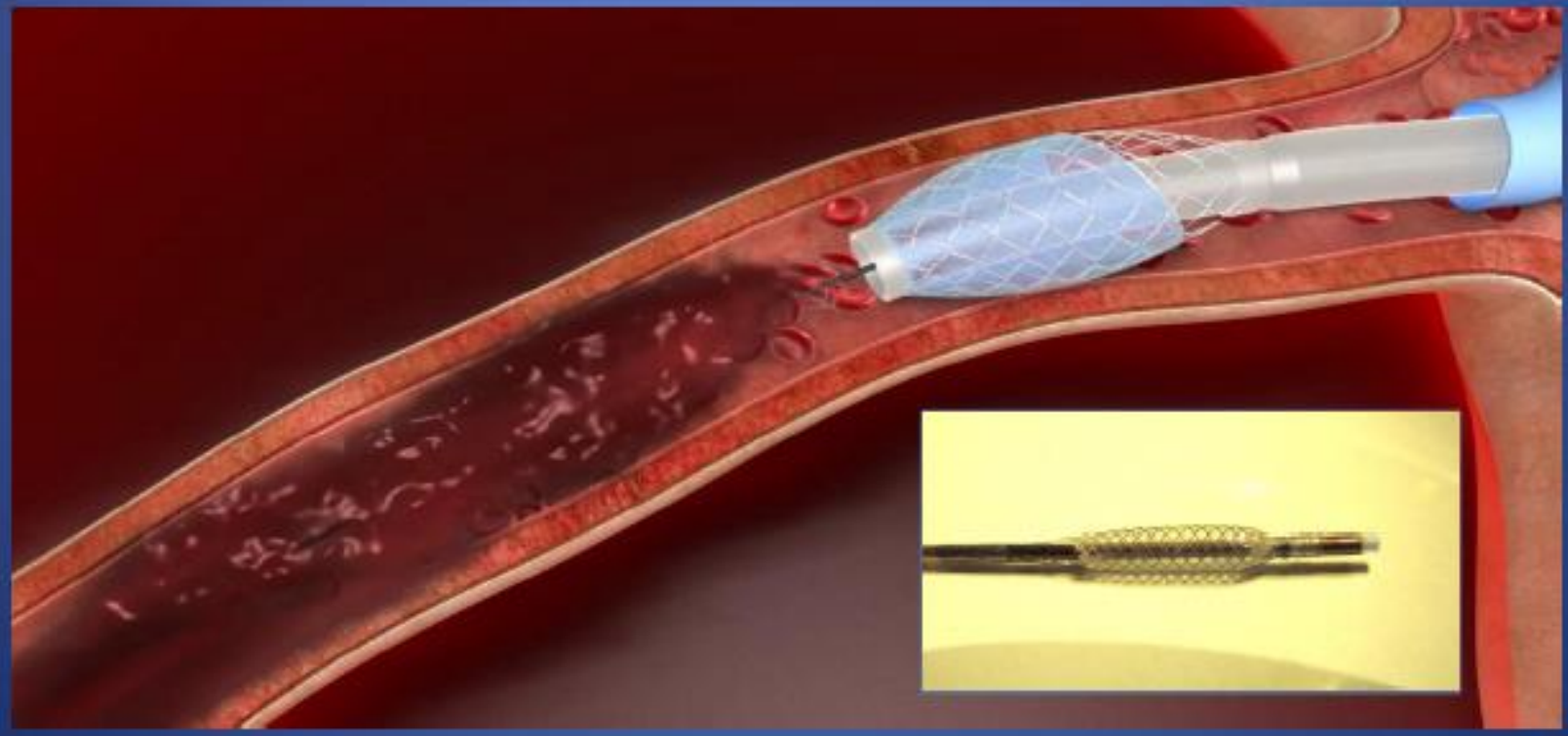
ESTABLISHED IN 1812 FEBRUARY 7, 2008 VOL. 358 NO. 6

Thrombus Aspiration during Primary Percutaneous Coronary Intervention

Tone Svilaas, M.D., Pieter J. Vlaar, M.Sc., Iwan C. van der Horst, M.D., Ph.D., Gilles F.H. Diercks, M.D., Ph.D., Bart J.G.L. de Smet, M.D., Ph.D., Ad F.M. van den Heuvel, M.D., Ph.D., Rutger L. Anthonio, M.D., Ph.D., Gillian A. Jessurun, M.D., Ph.D., Eng-Shiong Tan, M.D., Albert J.H. Suurmeijer, M.D., Ph.D., and Felix Zijlstra, M.D., Ph.D.

EmboPRO

A proximal embolic protection device. The first integrated solution offering simple and improved aspiration prior to PCI and embolic protection during PCI



2013

TASTE

ORIGINAL ARTICLE

Thrombus Aspiration during ST-Segment Elevation Myocardial Infarction

Ole Fröbert, M.D., Ph.D., Bo Lagerqvist, M.D., Ph.D., Göran K. Olivecrona, M.D., Ph.D., Elmir Omerovic, M.D., Ph.D., Thorarinn Gudnason, M.D., Ph.D., Michael Maeng, M.D., Ph.D., Mikael Aasa, M.D., Ph.D., Oskar Angerås, M.D., Fredrik Calais, M.D., Mikael Danielewicz, M.D., David Erlinge, M.D., Ph.D., Lars Hellsten, M.D., Ulf Jensen, M.D., Ph.D., Agneta C. Johansson, M.D., Amra Kåregren, M.D., Johan Nilsson, M.D., Ph.D., Lotta Robertson, M.D., Lennart Sandhall, M.D., Iwar Sjögren, M.D., Ollie Östlund, Ph.D., Jan Harnek, M.D., Ph.D., and Stefan K. James, M.D., Ph.D.

2015

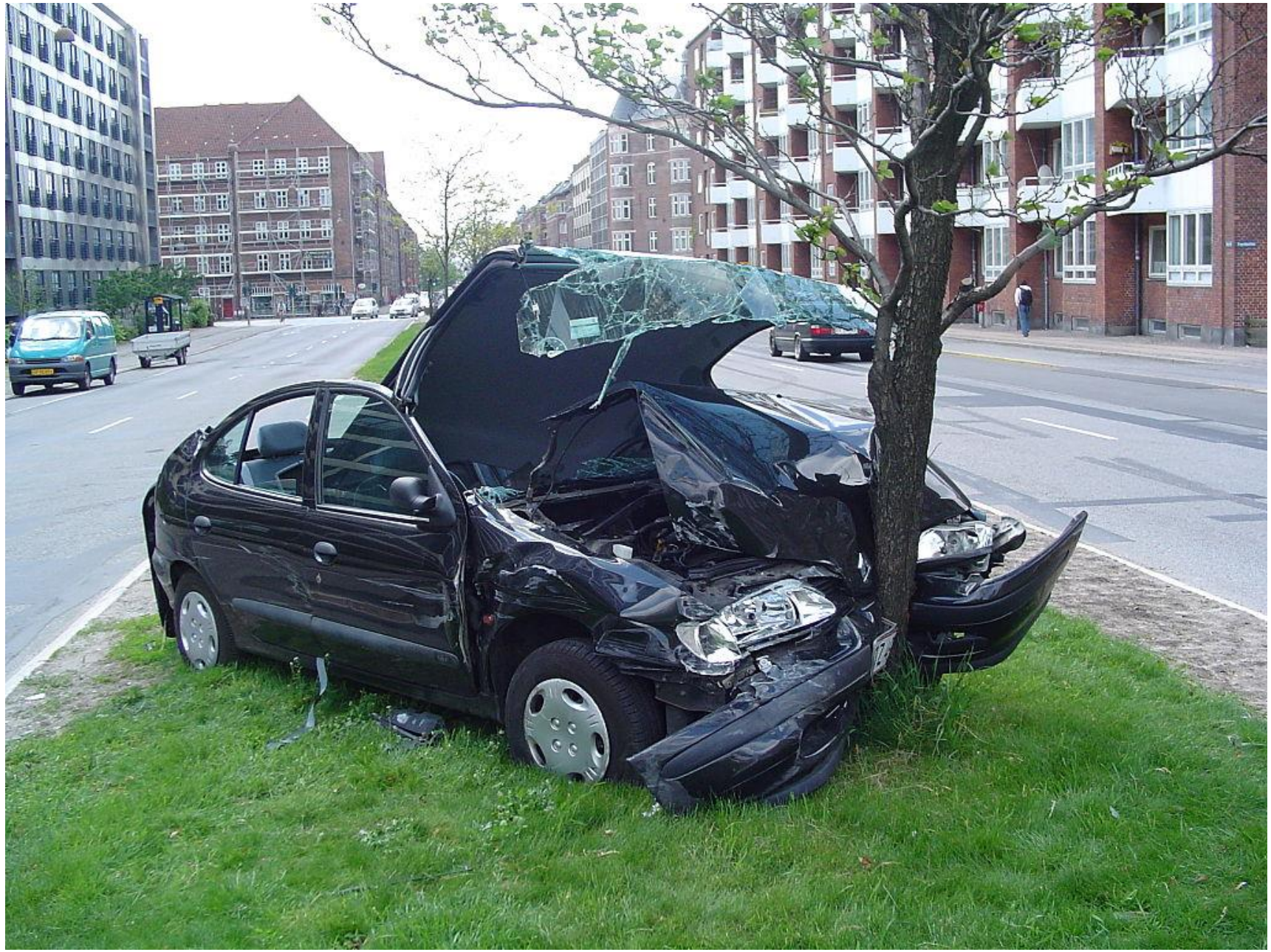
TOTAL

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 9, 2015 VOL. 372 NO. 15

Randomized Trial of Primary PCI with or without Routine Manual Thrombectomy

S.S. Jolly, J.A. Cairns, S. Yusuf, B. Meeks, J. Pogue, M.J. Rokoss, S. Kedev, L. Thabane, G. Stankovic, R. Moreno, A. Gershlick, S. Chowdhary, S. Lavi, K. Niemelä, P.G. Steg, I. Bernat, Y. Xu, W.J. Cantor, C.B. Overgaard, C.K. Naber, A.N. Cheema, R.C. Welsh, O.F. Bertrand, A. Avezum, R. Bhindi, S. Pancholy, S.V. Rao, M.K. Natarajan, J.M. ten Berg, O. Shestakovska, P. Gao, P. Widimsky, and V. Džavík, for the TOTAL Investigators*



MR CLEAN

2015

The NEW ENGLAND JOURNAL of MEDICINE

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A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke

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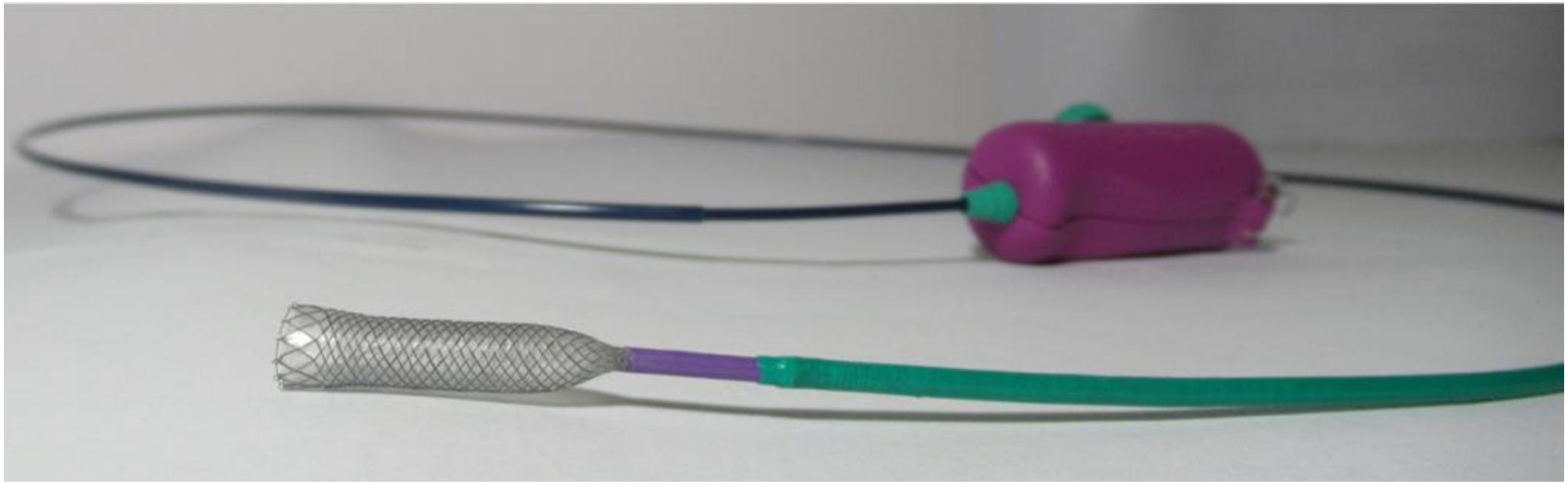
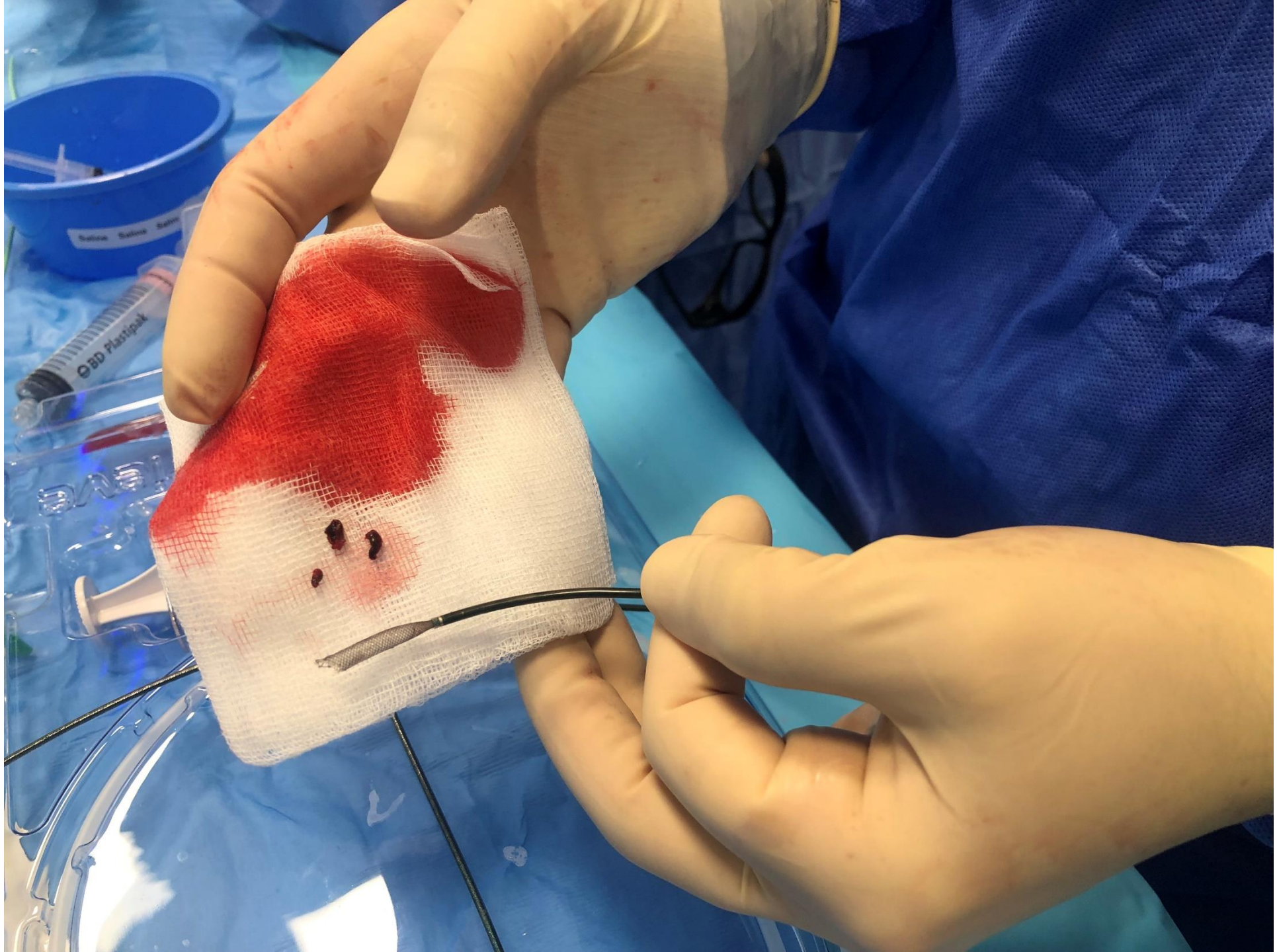
Ceretrieve

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