When Should We Consider MCS Before PCI in STEMI

Ziad A Ali MD DPhil
St Francis Hospital & Heart Center
Cardiovascular Research Foundation, New York, USA
zali@crf.org
Follow me @ziadalinyc

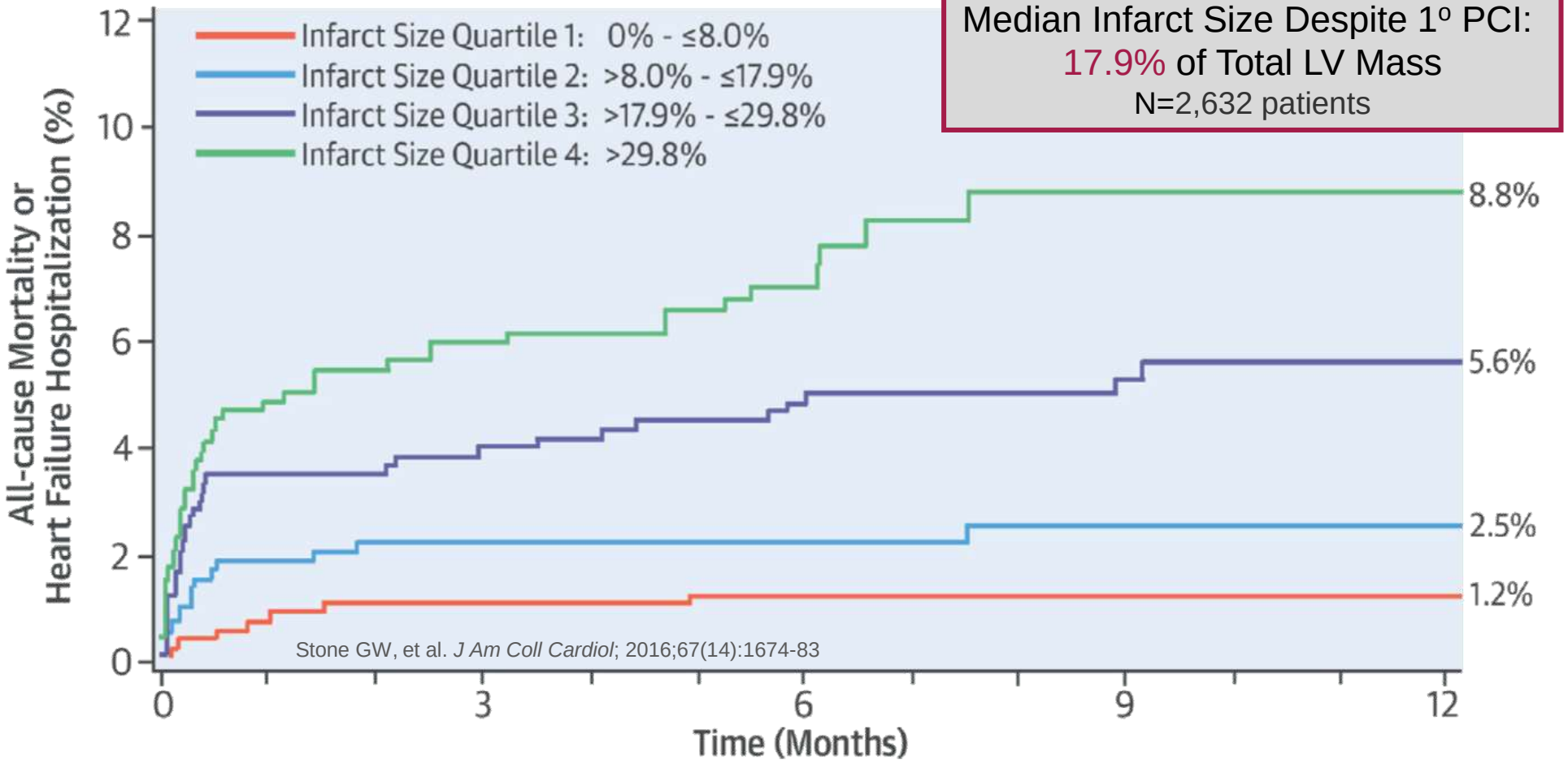
Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
Grant/Research Support (*Institutional*)	NIH/NHLBI, Abbott, Philips, Boston Scientific, Abiomed, Opsens, Acist Medical, Medtronic Cardiovascular Systems Inc
Consulting Fees/Honoraria	Amgen, Astra Zeneca, Boston Scientific
Equity	Shockwave Medical

Larger Infarcts Drive Mortality + HF

Median Infarct Size Despite 1º PCI:
17.9% of Total LV Mass
N=2,632 patients



For every 5% increase in myocardial infarct size, 1-year all-cause mortality increases by 19% & HF hospitalization by 20%

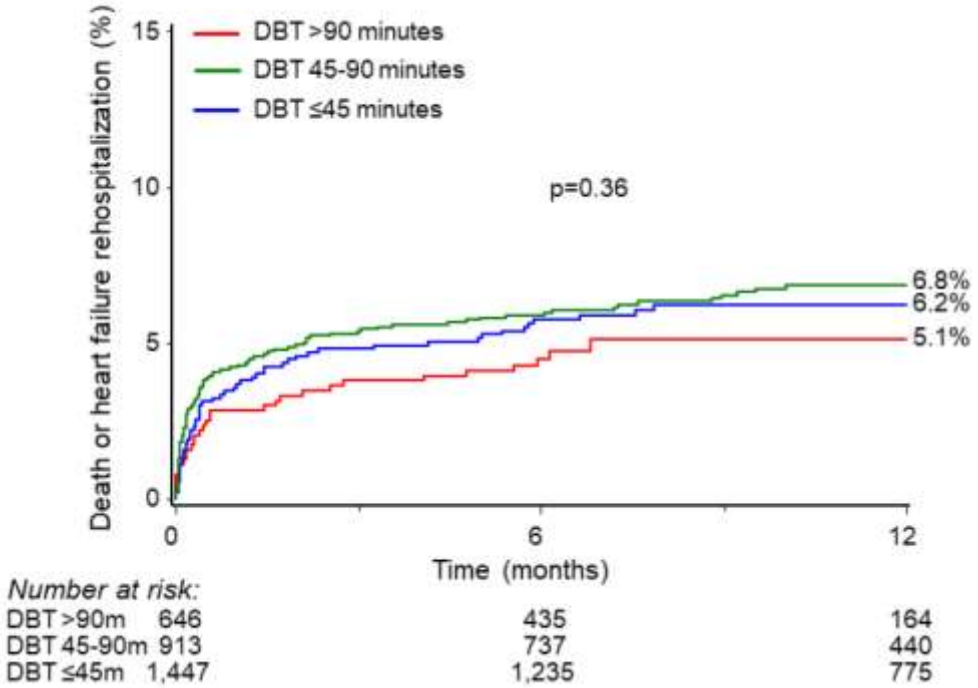
So how can we reduce infarct size?

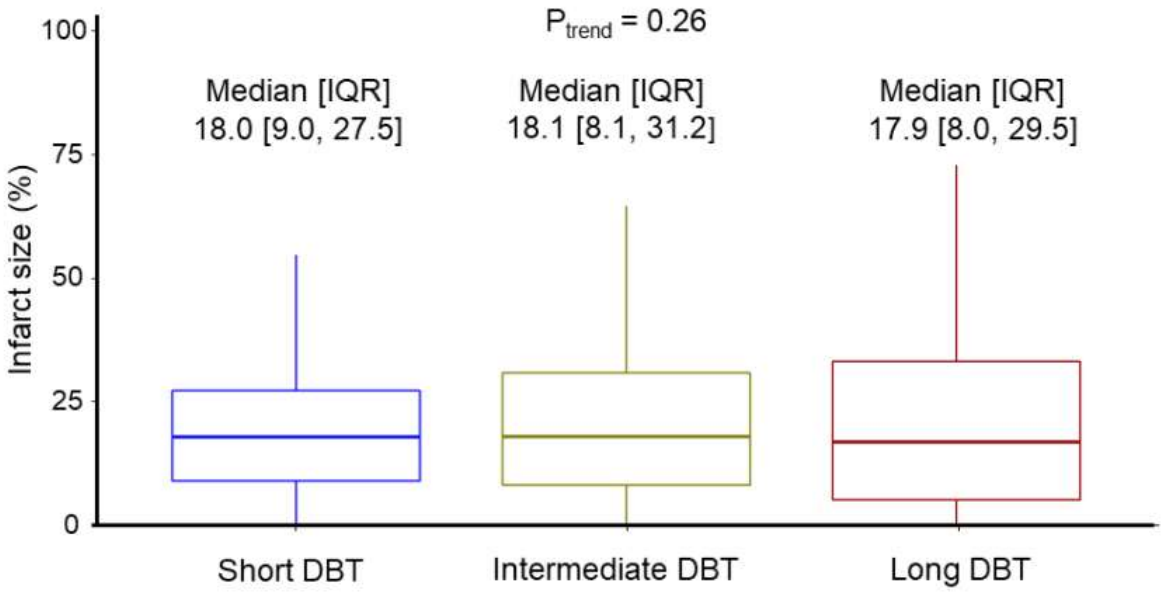
Time Delay, Infarct Size, and Microvascular Obstruction After Primary Percutaneous Coronary Intervention for ST-Segment–Elevation Myocardial Infarction

Björn Redfors, MD, PhD*; Reza Mohebi, MD*; Gennaro Giustino, MD; Shmuel Chen, MD, PhD; Harry P. Selker, MD, MSPH; Holger Thiele, MD; Manesh R. Patel, MD; James E. Udelson, MD; E. Magnus Ohman, MD; Ingo Eitel, MD; Christopher B. Granger, MD; Akiko Maehara, MD; Ziad A. Ali, MD, DPhil; Ori Ben-Yehuda, MD; Gregg W. Stone, MD

Door-to-balloon time						
>90 min vs ≤45 min	1.01 (0.61–1.67)	0.96	1.07 (0.60–1.92)	0.82	0.67 (0.31–1.46)	0.32
45–90 min vs ≤45 min	1.03 (0.70–1.50)	0.90	0.91 (0.57–1.46)	0.71	1.03 (0.61–1.74)	0.91
Per 10-min increase	1.02 (0.98–1.06)	0.28	1.02 (0.98–1.07)	0.23	0.99 (0.93–1.05)	0.78

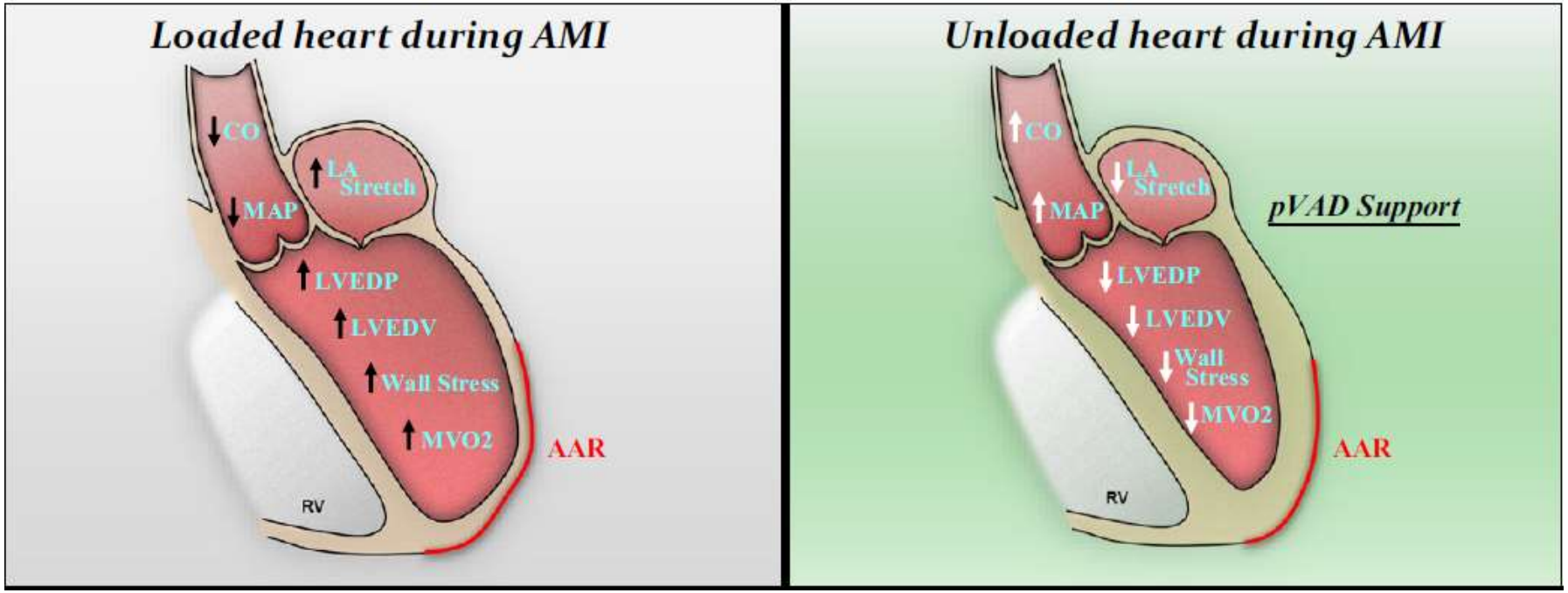
Values are hazard ratio (95% CI). The multivariable models were adjusted for the following covariate set: Age, sex, hypertension, hyperlipidemia, current smoking, LAD vs non-LAD infarct artery, and prior myocardial infarction. LAD indicates left anterior descending.





What about unloading?

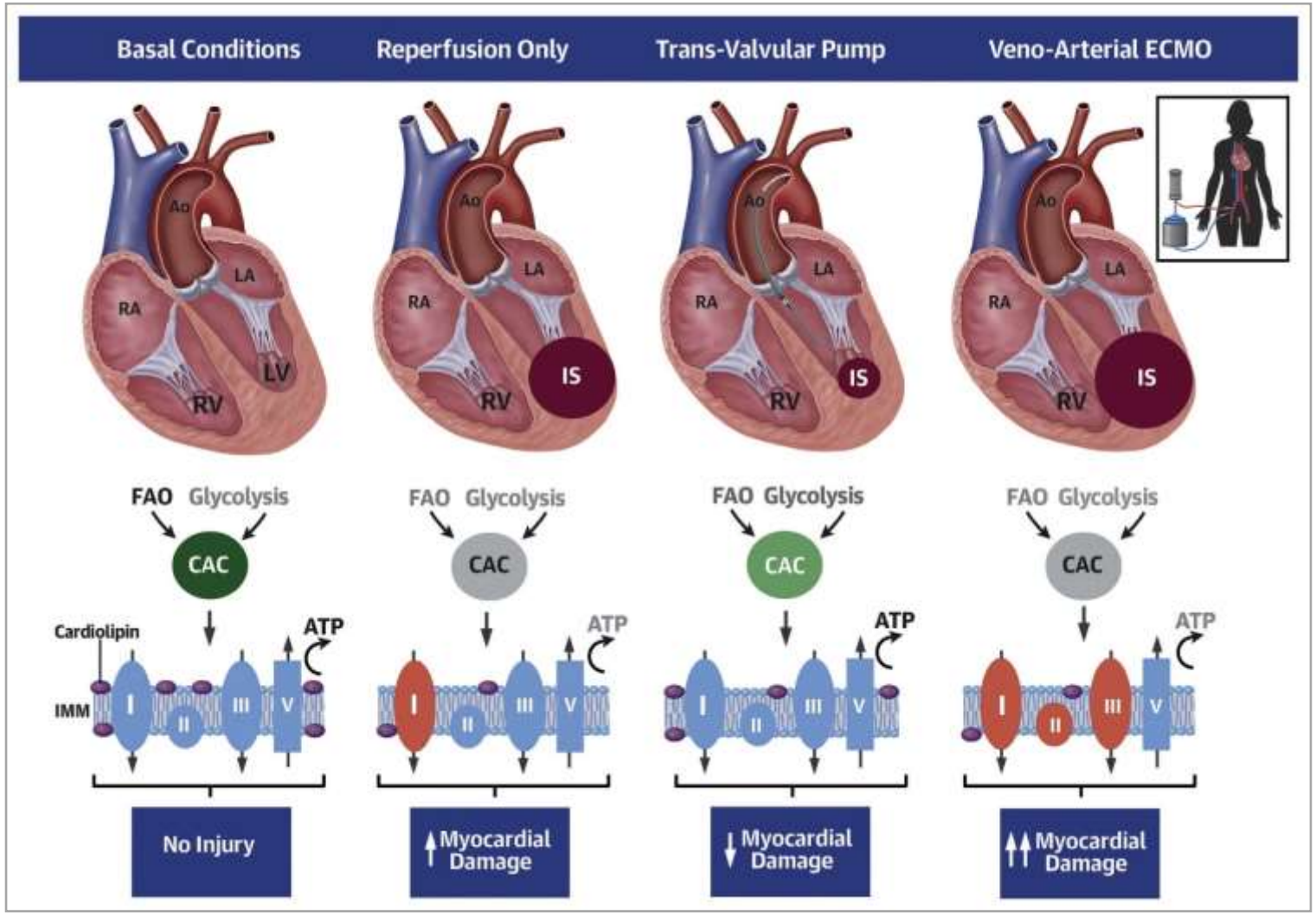
UNLOADING – THE SCIENCE



- Decreased myocardial oxygen consumption
- Activation of cardioprotective signaling
- Increased cardiac microvascular perfusion into infarct zone
- Hemodynamic stabilization through reperfusion-dependent arrhythmia
- Bridge through reperfusion-induced myocardial stunning
- Reduced acute infarct size and subsequent scar size

Curran J, et al. *Journal of Cardiovascular Translational Research* 2019;(12):95–106

CHOICES

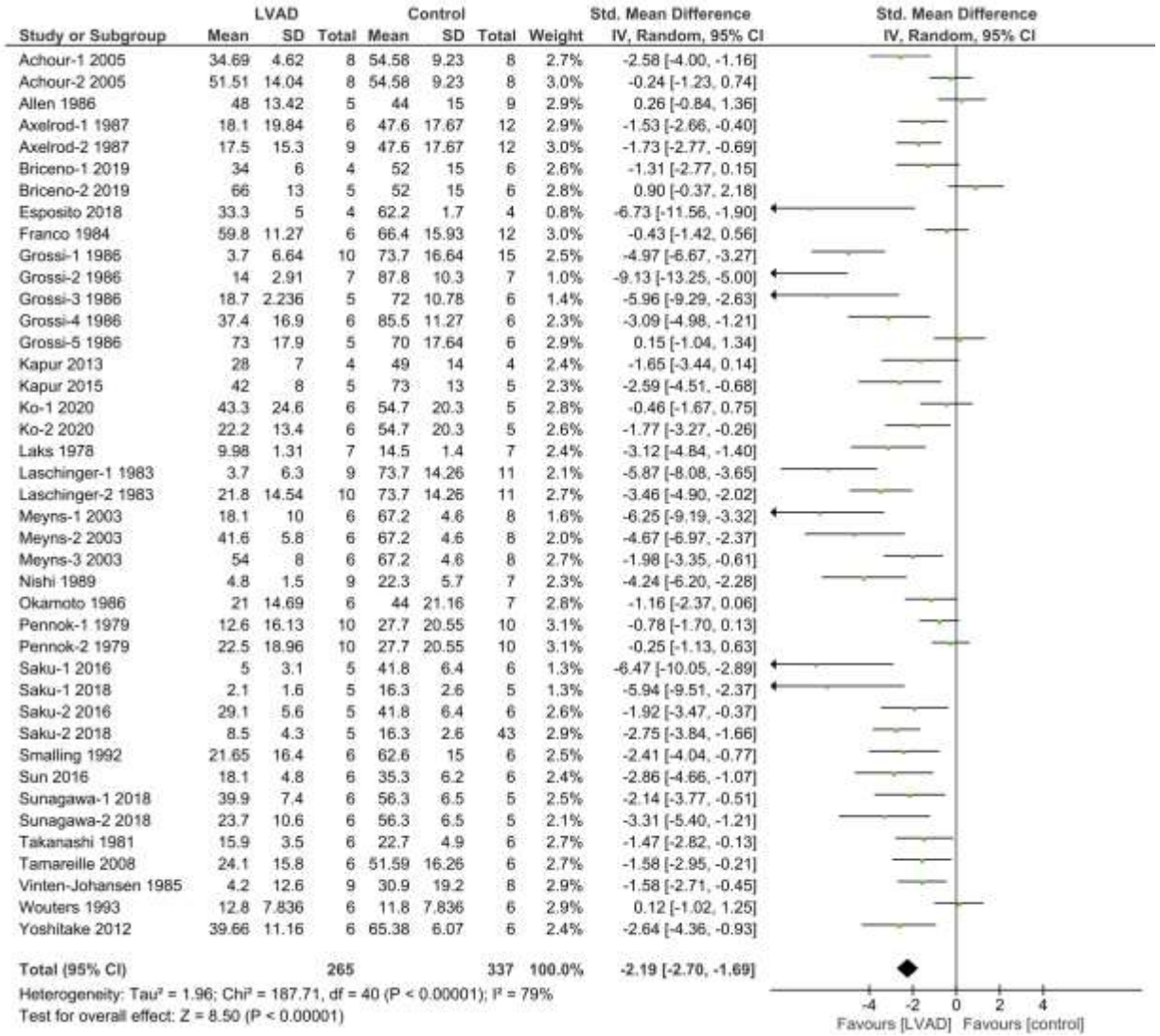


Swain L, Kapur N, et al. *J Am Coll Cardiol*. 2020;76(6):684-699.

Is there evidence for unloading?

But that’s just basic science…

LV Unloading has Data to Support it?



Study or Subgroup	LVAD Mean	LVAD SD	LVAD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Achour-1 2005	34.69	4.62	8	54.58	9.23	8	2.7%	-2.58 [-4.00, -1.16]
Achour-2 2005	51.51	14.04	8	54.58	9.23	8	3.0%	-0.24 [-1.23, 0.74]
Allen 1986	48	13.42	5	44	15	9	2.9%	0.26 [-0.84, 1.36]
Axelrod-1 1987	18.1	19.84	6	47.6	17.67	12	2.9%	-1.53 [-2.66, -0.40]
Axelrod-2 1987	17.5	15.3	9	47.6	17.67	12	3.0%	-1.73 [-2.77, -0.69]
Briceno-1 2019	34	6	4	52	15	6	2.6%	-1.31 [-2.77, 0.15]
Briceno-2 2019	66	13	5	52	15	6	2.8%	0.90 [-0.37, 2.18]
Esposito 2018	33.3	5	4	62.2	1.7	4	0.8%	-6.73 [-11.56, -1.90]
Franco 1984	59.8	11.27	6	66.4	15.93	12	3.0%	-0.43 [-1.42, 0.56]
Grossi-1 1986	3.7	6.64	10	73.7	16.64	15	2.5%	-4.97 [-6.67, -3.27]
Grossi-2 1986	14	2.91	7	87.8	10.3	7	1.0%	-9.13 [-13.25, -5.00]
Grossi-3 1986	18.7	2.236	5	72	10.78	6	1.4%	-5.96 [-9.29, -2.63]
Grossi-4 1986	37.4	16.9	6	85.5	11.27	6	2.3%	-3.09 [-4.98, -1.21]
Grossi-5 1986	73	17.9	5	70	17.64	6	2.9%	0.15 [-1.04, 1.34]
Kapur 2013	28	7	4	49	14	4	2.4%	-1.65 [-3.44, 0.14]
Kapur 2015	42	8	5	73	13	5	2.3%	-2.59 [-4.51, -0.68]
Ko-1 2020	43.3	24.6	6	54.7	20.3	5	2.8%	-0.46 [-1.67, 0.75]
Ko-2 2020	22.2	13.4	6	54.7	20.3	5	2.6%	-1.77 [-3.27, -0.26]
Laks 1978	9.98	1.31	7	14.5	1.4	7	2.4%	-3.12 [-4.84, -1.40]
Laschinger-1 1983	3.7	6.3	9	73.7	14.26	11	2.1%	-5.87 [-8.08, -3.65]
Laschinger-2 1983	21.8	14.54	10	73.7	14.26	11	2.7%	-3.46 [-4.90, -2.02]
Meyns-1 2003	18.1	10	6	67.2	4.6	8	1.6%	-6.25 [-9.19, -3.32]
Meyns-2 2003	41.6	5.8	6	67.2	4.6	8	2.0%	-4.67 [-6.97, -2.37]
Meyns-3 2003	54	8	6	67.2	4.6	8	2.7%	-1.98 [-3.35, -0.61]
Nishi 1989	4.8	1.5	9	22.3	5.7	7	2.3%	-4.24 [-6.20, -2.28]
Okamoto 1986	21	14.69	6	44	21.16	7	2.8%	-1.16 [-2.37, 0.06]
Pennok-1 1979	12.6	16.13	10	27.7	20.55	10	3.1%	-0.78 [-1.70, 0.13]
Pennok-2 1979	22.5	18.96	10	27.7	20.55	10	3.1%	-0.25 [-1.13, 0.63]
Saku-1 2016	5	3.1	5	41.8	6.4	6	1.3%	-6.47 [-10.05, -2.89]
Saku-1 2018	2.1	1.6	5	16.3	2.6	5	1.3%	-5.94 [-9.51, -2.37]
Saku-2 2016	29.1	5.6	5	41.8	6.4	6	2.6%	-1.92 [-3.47, -0.37]
Saku-2 2018	8.5	4.3	5	16.3	2.6	43	2.9%	-2.75 [-3.84, -1.66]
Smalling 1992	21.65	16.4	6	62.6	15	6	2.5%	-2.41 [-4.04, -0.77]
Sun 2016	18.1	4.8	6	35.3	6.2	6	2.4%	-2.86 [-4.66, -1.07]
Sunagawa-1 2018	39.9	7.4	6	56.3	6.5	5	2.5%	-2.14 [-3.77, -0.51]
Sunagawa-2 2018	23.7	10.6	6	56.3	6.5	5	2.1%	-3.31 [-5.40, -1.21]
Takanashi 1981	15.9	3.5	6	22.7	4.9	6	2.7%	-1.47 [-2.82, -0.13]
Tamareille 2008	24.1	15.8	6	51.59	16.26	6	2.7%	-1.58 [-2.95, -0.21]
Vinten-Johansen 1985	4.2	12.6	9	30.9	19.2	8	2.9%	-1.58 [-2.71, -0.45]
Wouters 1993	12.8	7.836	6	11.8	7.836	6	2.9%	0.12 [-1.02, 1.25]
Yoshitake 2012	39.66	11.16	6	65.38	6.07	6	2.4%	-2.64 [-4.36, -0.93]
Total (95% CI)			**265**			**337**	**100.0%**	**-2.19 [-2.70, -1.69]**

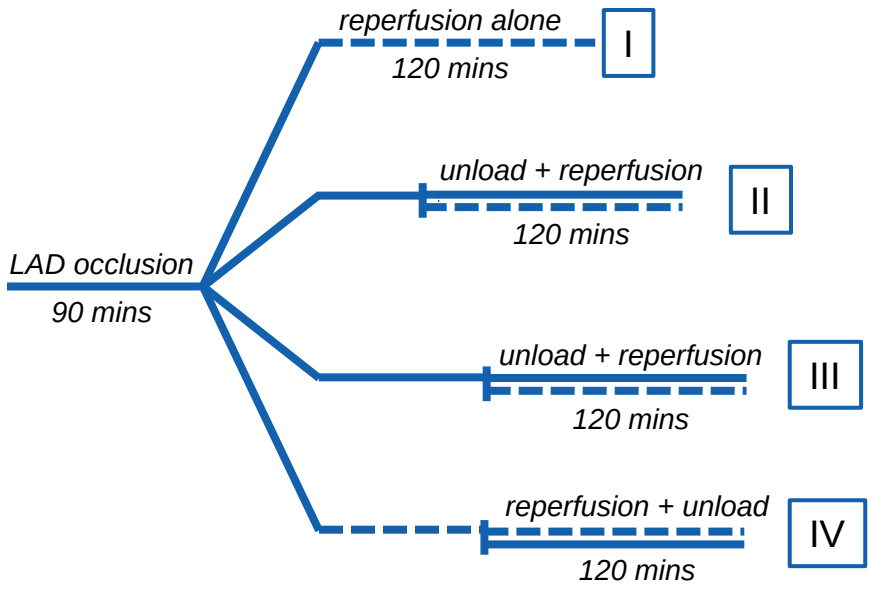
Heterogeneity: Tau² = 1.96; Chi² = 187.71, df = 40 (P < 0.00001); I² = 79%
Test for overall effect: Z = 8.50 (P < 0.00001)

Miyashita S, Kapur NK, Ishikawa K, et al. J of Cardiovasc Trans Res. 2021;14:467-475.

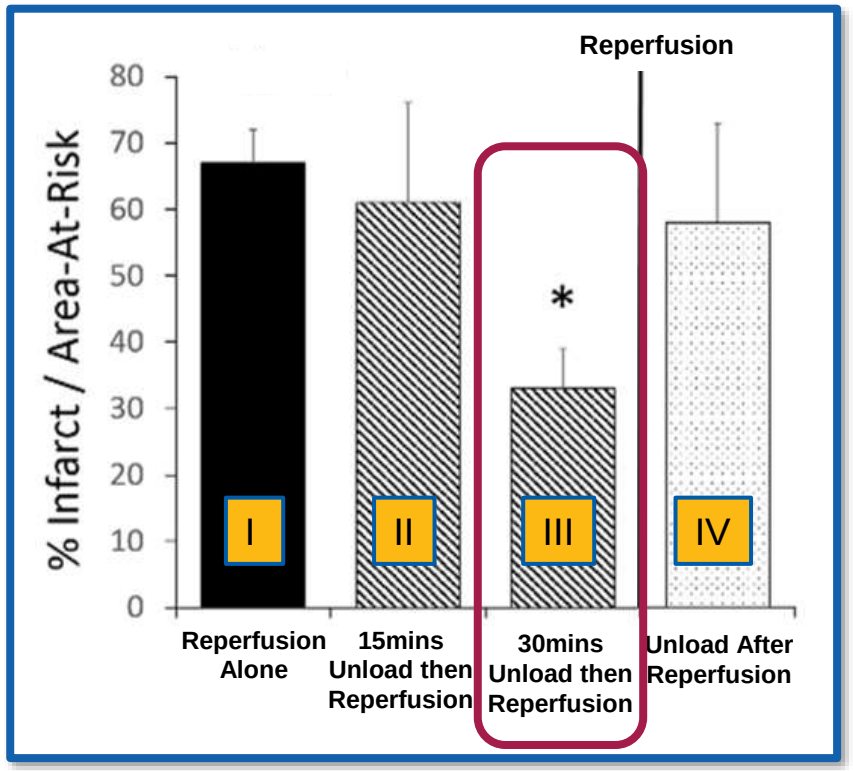
What's next?

Unloading 30mins Before Reperfusion Demonstrated Strongest Cardioprotective Effect

Experimental Design

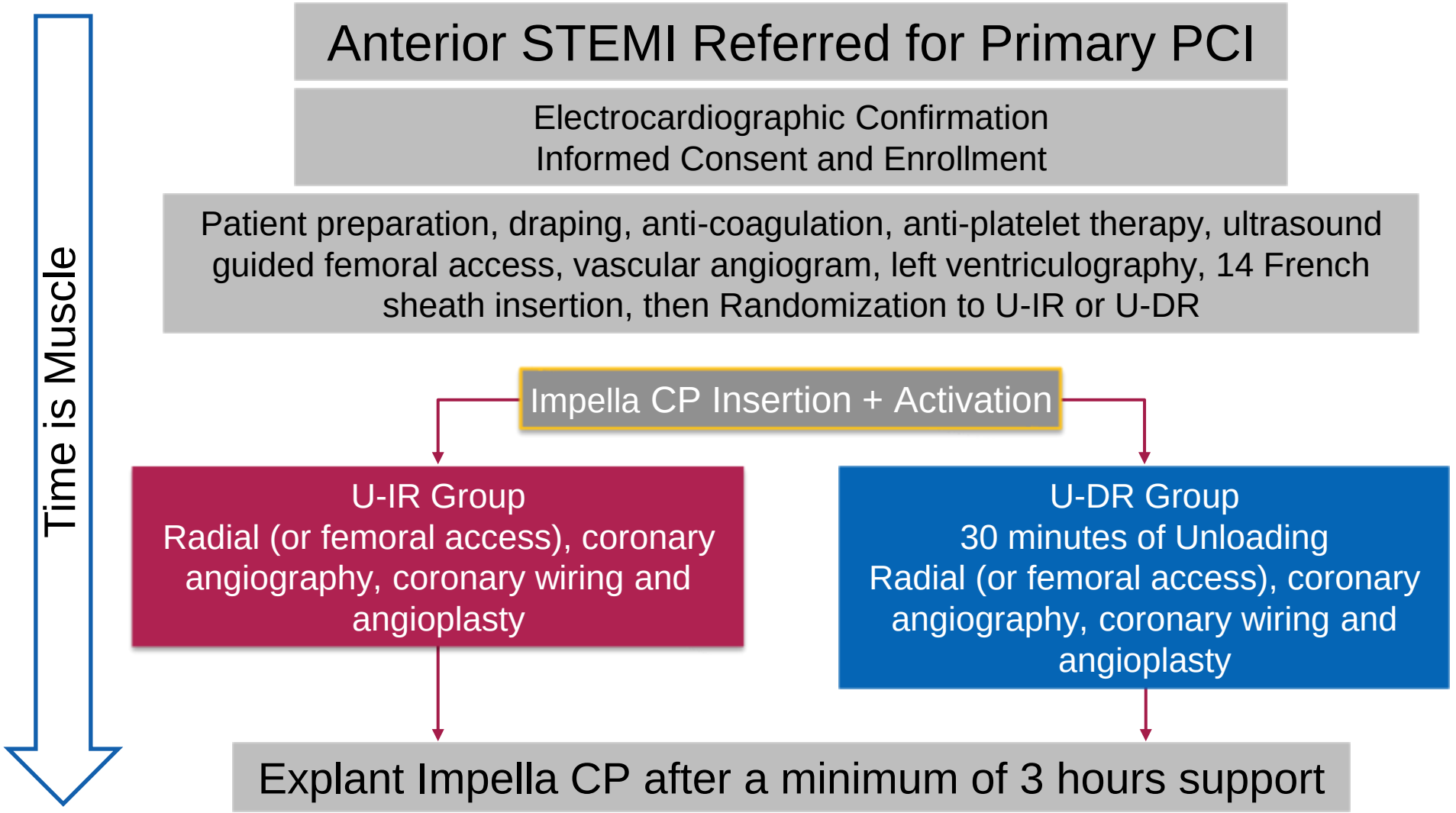


Results: Infarct Size / Area-at-Risk (AAR)



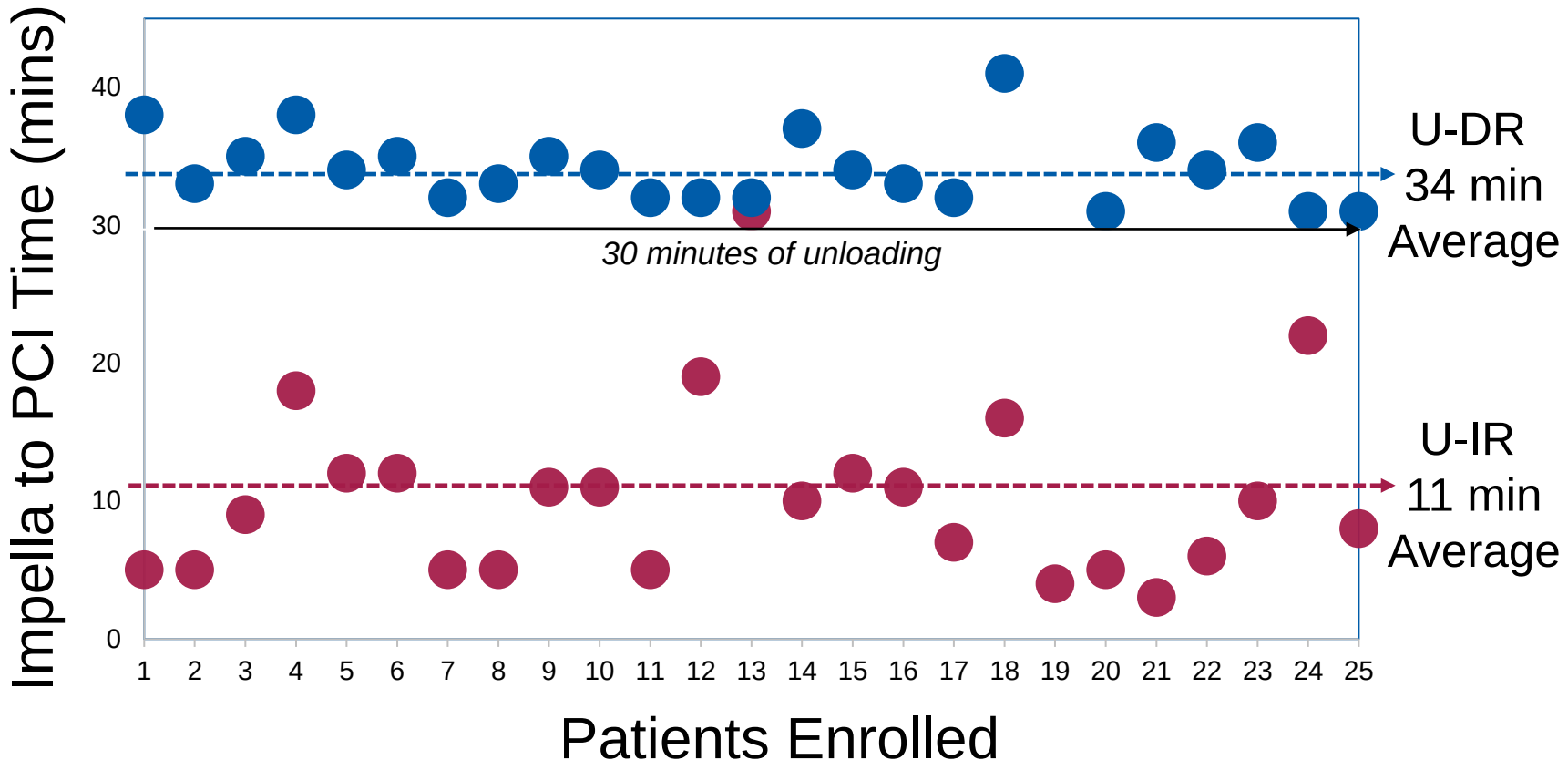
Esposito M, et al. *JACC;* 2018

DOOR-TO-UNLOAD: STEMI PILOT TRIAL STUDY DESIGN



Independent Data Safety Monitor, Electrocardiographic, Angiographic and Cardiac Magnetic Resonance Imaging Core Labs

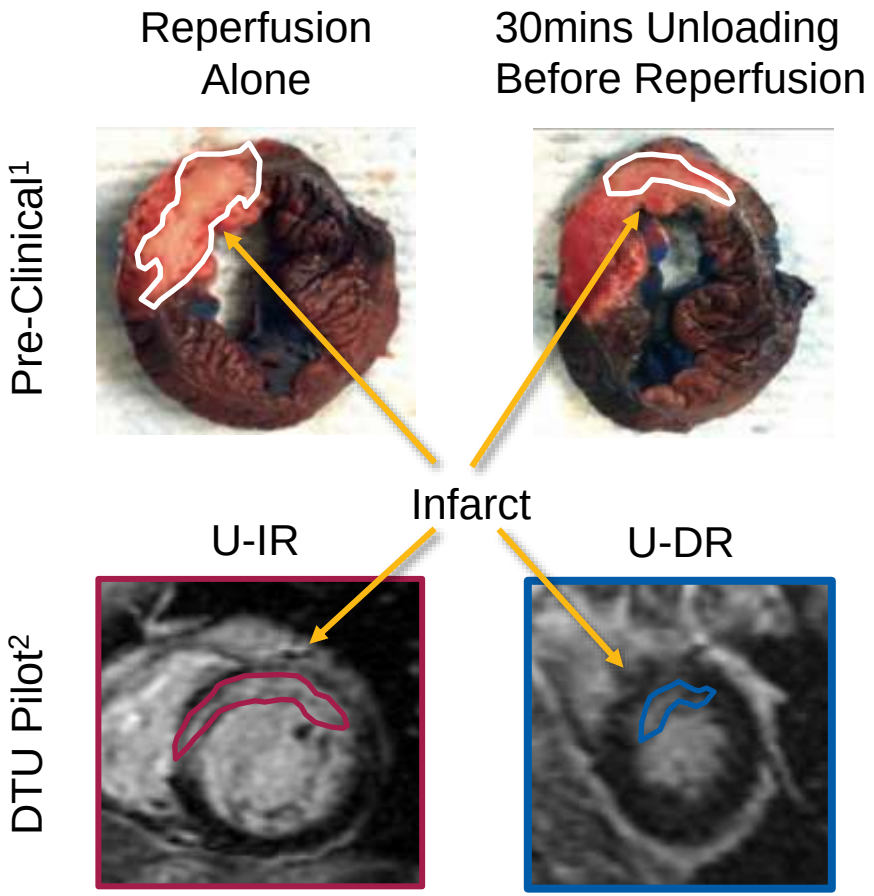
Successful Enrollment & Protocol Completion Zero Bail-Out PCI in the U-DR Group



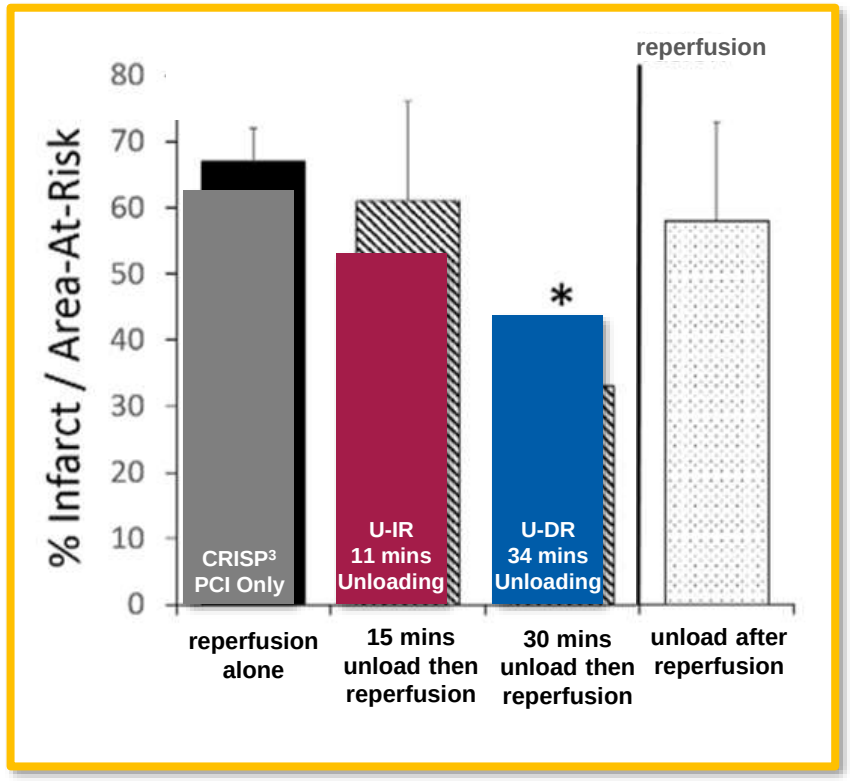
U-IR Unloading followed by Immediate Reperfusion
U-DR Unloading for 30 minutes with Delayed Reperfusion

Kapur, et al. *Circulation*. 2019;139:337–346

Successful Translation from Pre-Clinical to Patients



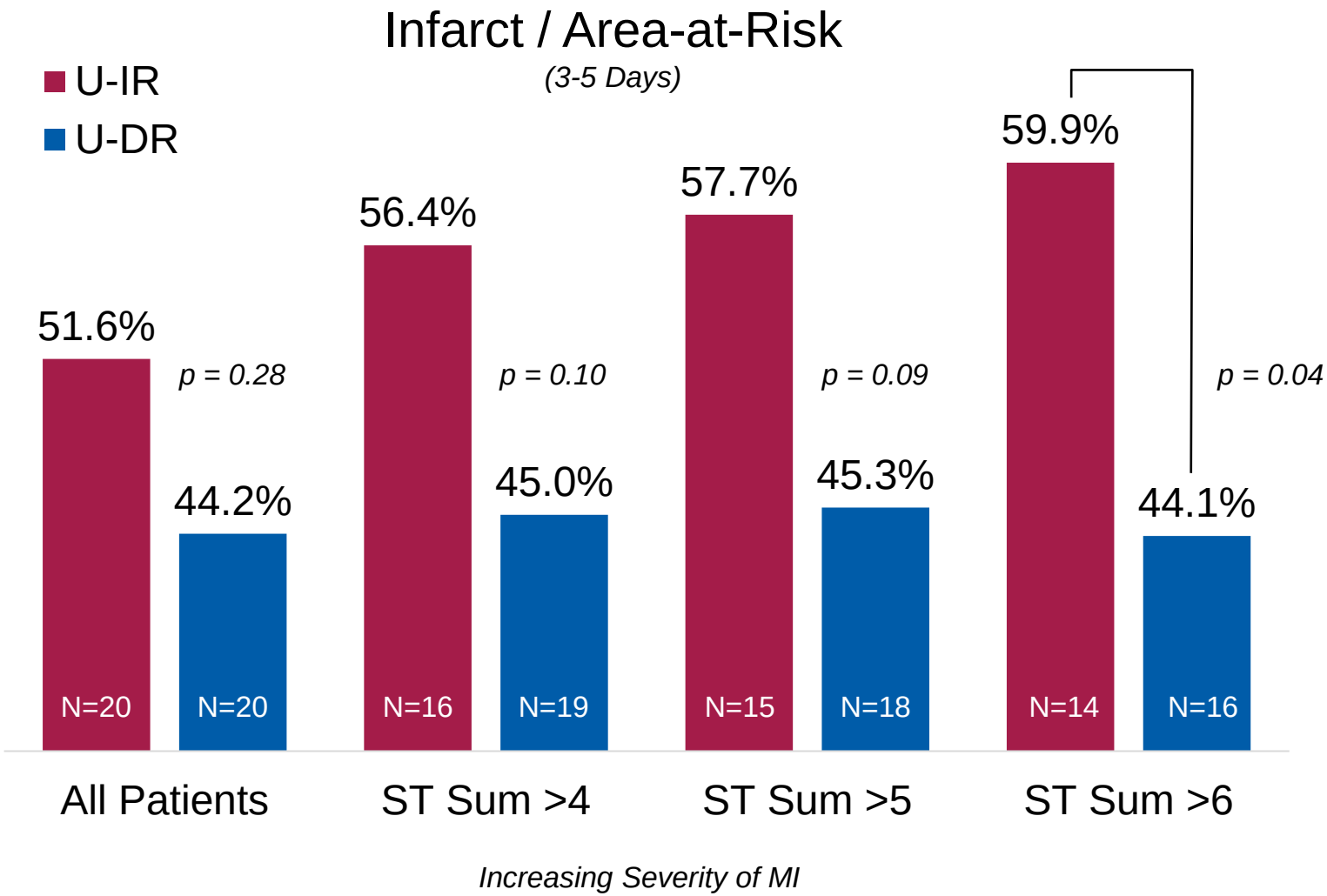
Infarct Size / Area at Risk (AAR)



U-IR Unloading followed by Immediate Reperfusion
U-DR Unloading for 30 minutes with Delayed Reperfusion

1. Esposito M, et al. *JACC*; 2018
2. Kapur N, et al. *Circulation Ahead of Print;* 2018, 10.1161
3. Patel M, et al. *JAMA;* 2011

30MINS UNLOADING DECOUPLES INFARCT SIZE FROM SEVERITY OF MI



U-IR Unloading followed by Immediate Reperfusion
U-DR Unloading for 30 minutes with Delayed Reperfusion

Kapur, et al. *Circulation Supplemental Appendix;* 2018, 10.1161

Safety Outcomes

Clinical Variable	U-IR (n=25)	U-DR (n=25)	p-value
CV Mortality, n (%)	1 (4%)	1 (4%)	NS
Reinfarction, n (%)	0	0	NS
Stroke or TIA, n (%)	1 (4%)	0	NS
Traditional 30-Day MACCE, n (%)	2 (8%)	1 (4%)	NS
Major Vascular Events, n (%)	0	2 (8%)	NS
Bleeding (BARC ≥ 2)	3 (12%)	4 (16%)	NS
Bleeding Requiring Transfusion	2 (8%)	1 (4%)	NS
Aortic Valve Injury	0	0	NS
Acute Renal Dysfunction	1 (4%)	1 (4%)	NS
Hemolysis	1 (4%)	0	NS

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Traditional 30-Day MACCE, n (%)	2 (8%)	1 (4%)	NS
Major Vascular Events, n (%)	0	2 (8%)	NS
Total 30-Day Composite MACCE, n (%)	2 (8%)	3 (12%)	NS

CV Mortality → **POOR PATIENT SELECTION**

- One mortality on POD 24 due to chronic lung disease
- One mortality due to shock on admission

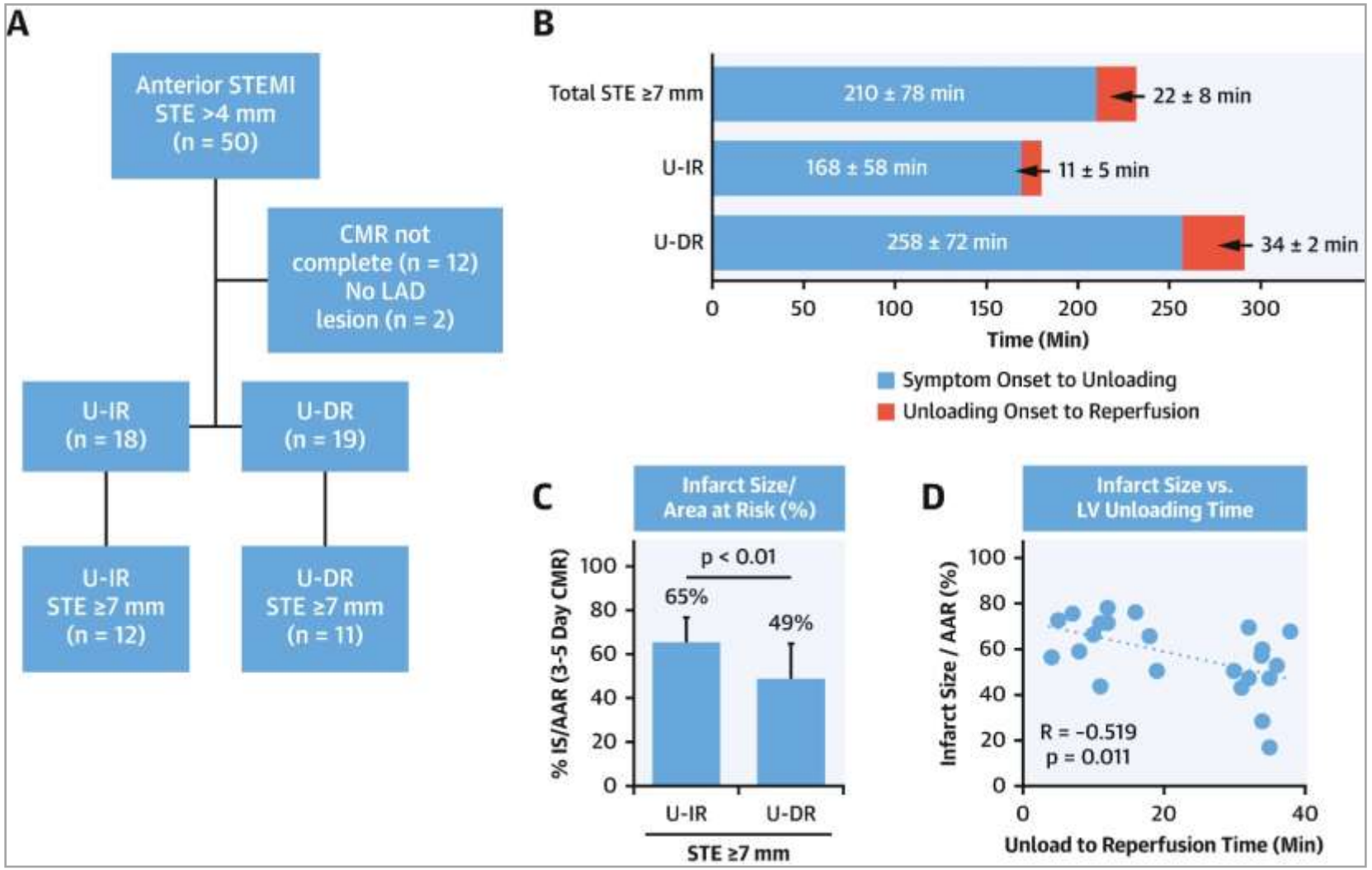
Major Vascular Events → **PREVENTABLE VASCULAR INJURY**

- Two iliofemoral dissection at the time of device removal

Kapur, et al. *Circulation.* 2019;139:337-346

U-IR Unloading followed by Immediate Reperfusion
U-DR Unloading for 30 minutes with Delayed Reperfusion

Large Anterior MI's Benefit from Unloading Irrespective of DTB Time



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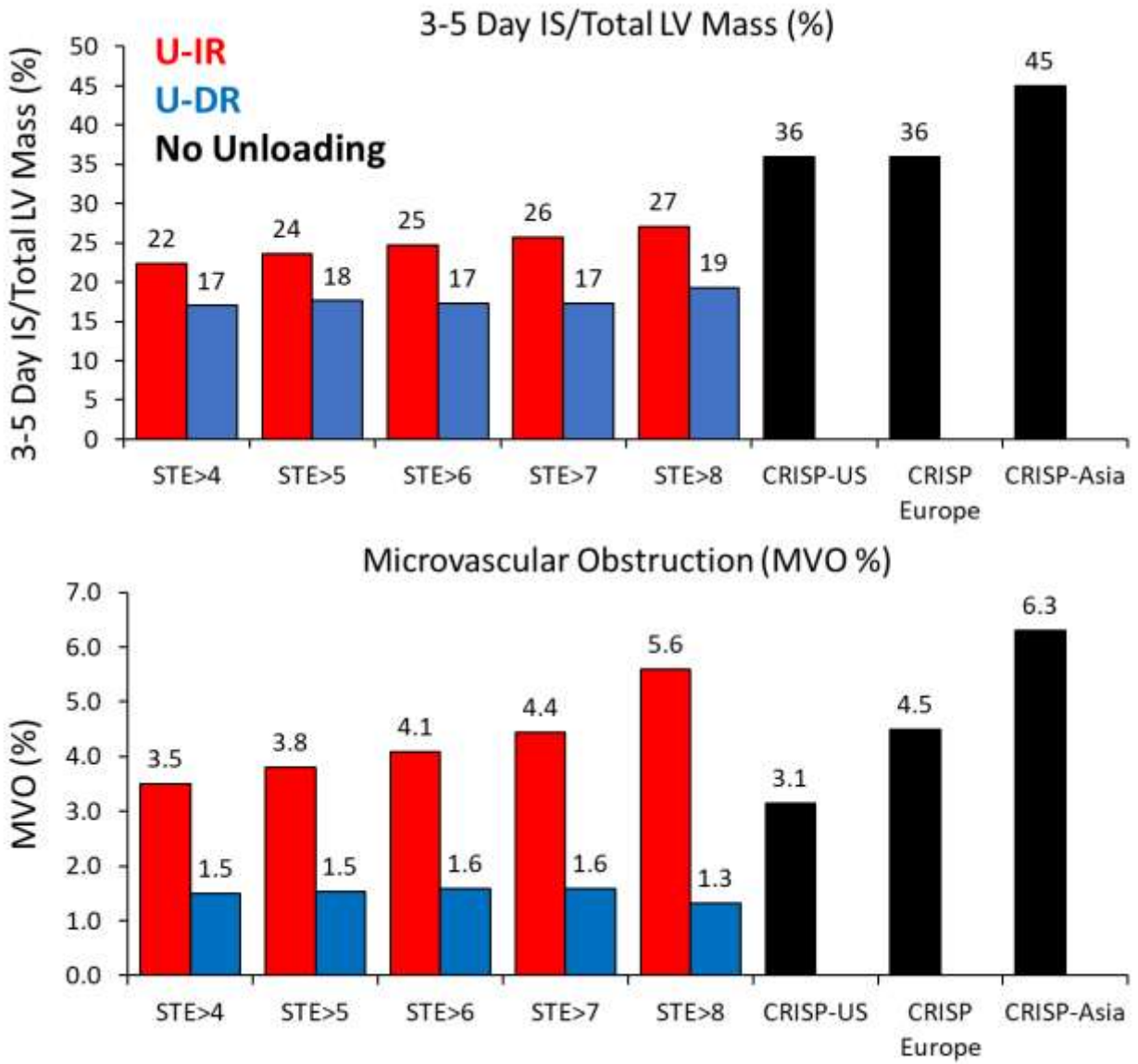
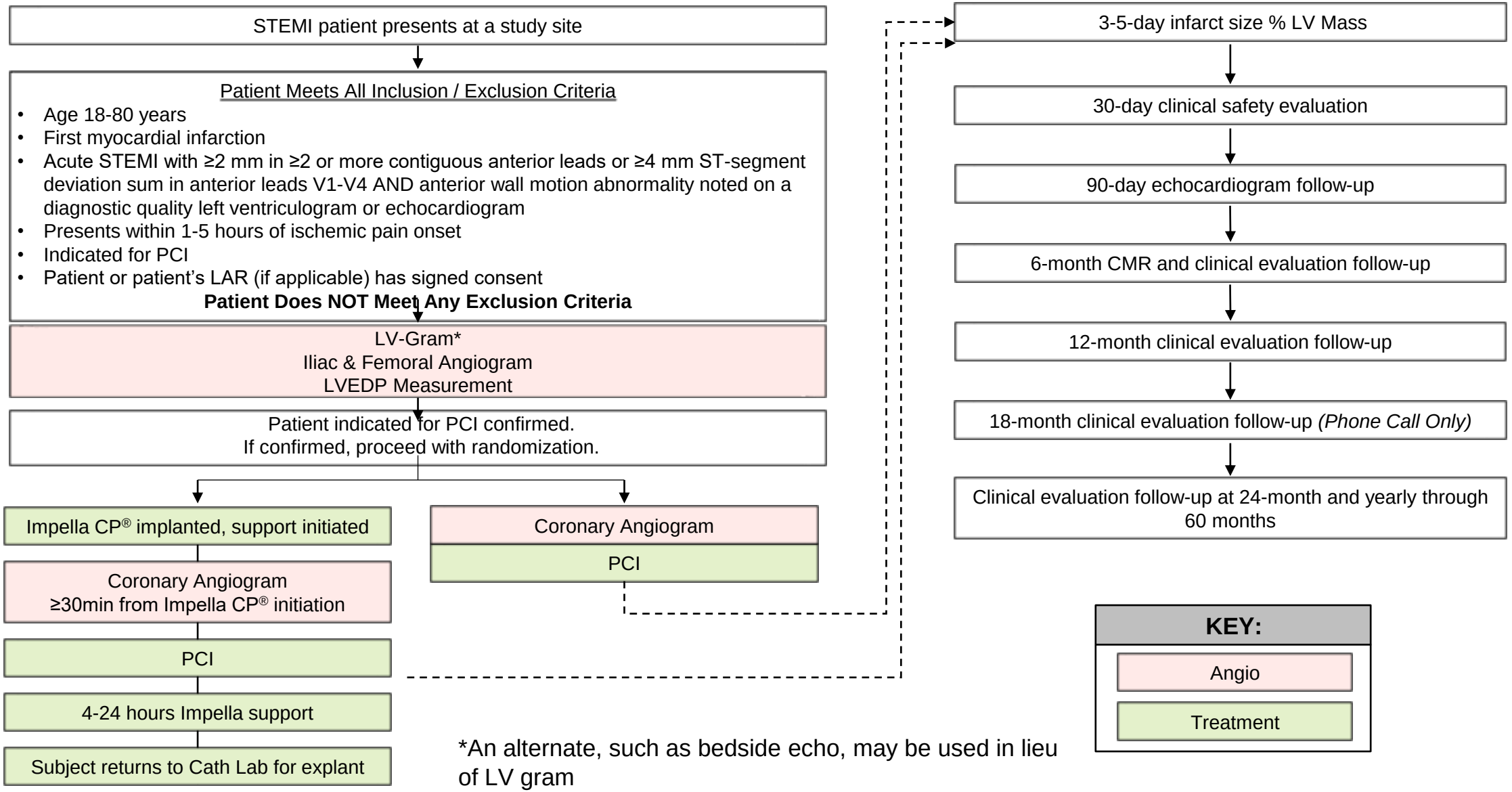
DTU Pilot Per-Protocol Analysis



STEMI DTU



*An alternate, such as bedside echo, may be used in lieu of LV gram