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Multivessel PCI in AMI and Cardiogenic Shock: SHOCK Trial Series Review and Real-World Application

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Disclosure Statement of Financial Interest

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

Affiliation/Financial relationship	Company
Speakers' honoraria	AstraZeneca, Abbott Vascular, Bayer, Sanofi Aventis
Consulting	Abbott Vascular, Bayer
Advisory Board	Abbott Vascular, AstraZeneca, Bayer

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Key Lessons in AMI with Cardiogenic Shock
1. Early Revascularization Reduces Mortality

SHOCK trial: 302 patients with STEMI and cardiogenic shock randomized to either revascularization (accomplished by CABG or angioplasty) or medical therapy

Outcome and subgroup	Revascularization	Medical therapy	Relative risk (95% CI)	P Value
30-day death	46.7%	56.0%	0.83 (0.67-1.04)	0.11
6-month death	50.3%	63.1%	0.80 (0.65-0.98)	**0.027**

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Hockman JS, et al. N Engl J Med. 1999;341:625-34

Key Lessons in AMI with Cardiogenic Shock
2. IABP Does Not Reduce Mortality

IABP-SHOCK II: 600 patients with AMI and cardiogenic shock undergoing early revascularization randomized to either IABP or not IAPB

Outcome and subgroup	IABP	No IABP	Relative risk (95% CI)	P Value
30-day death	39.7%	41.3%	0.96 (0.79-1.17)	0.69

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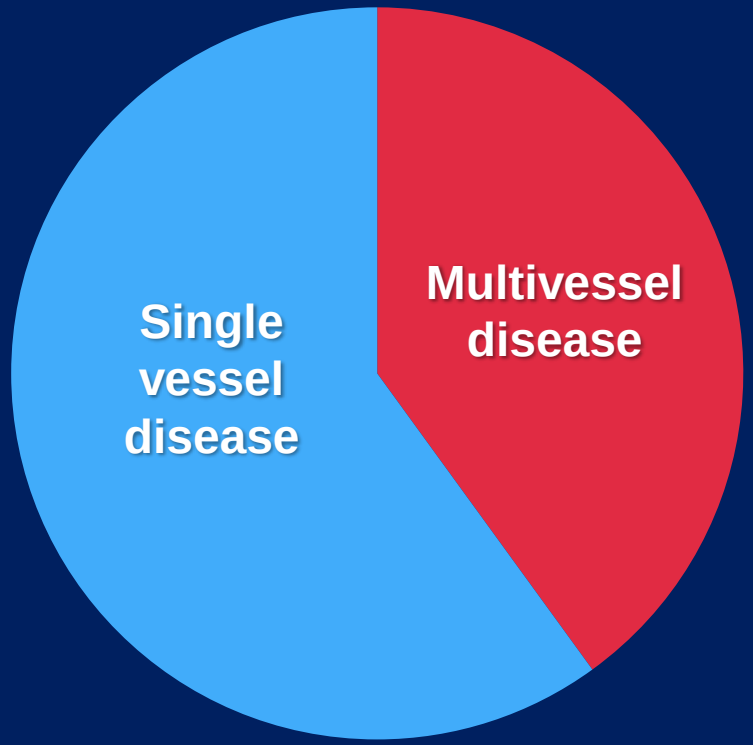
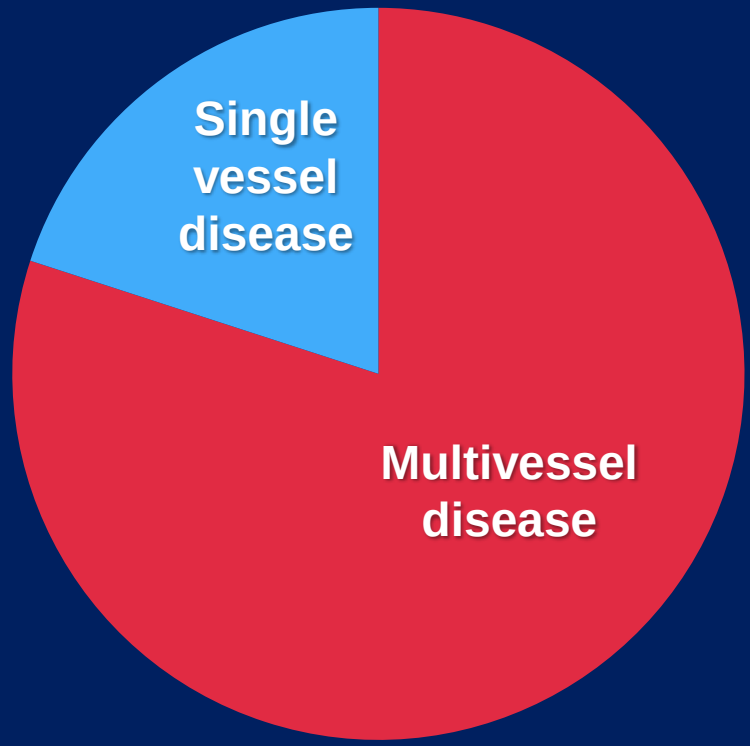
Thiele H, et al. N Engl J Med. 2012;367:1287-96

Multivessel Disease in Acute Myocardial Infarction

STEMI without cardiogenic shock



STEMI with cardiogenic shock



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Lee JM, et al. J Am Coll Cardiol. 2018;71:844-856

Recommendations for Multivessel PCI With Acute Myocardial Infarction With Cardiogenic Shock

2017 ESC Guidelines for ST-segment Elevation Myocardial Infarction

Recommendation	Class	LOE
Non-IRA PCI during the index procedure should be considered in patients with cardiogenic shock.	IIa	C

Ibanez B, et al. Eur Heart J. 2018;39:119-177

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Recommendations for Multivessel PCI With Acute Myocardial Infarction WITHOUT Cardiogenic Shock

2017 ESC Guidelines for ST-segment Elevation Myocardial Infarction

Recommendation	Class	LOE
Routine revascularization of non-IRA lesions should be considered in STEMI patients with multivessel disease before hospital discharge.	IIa	A

- Politi et al. Heart 2010
- PRAMI NEJM 2013
- CvLPRIT JACC 2015
- DANAMI 3 Lancet 2015
- COMPARE-ACUTE NEJM 2017

Ibanez B, et al. Eur Heart J. 2018;39:119-177

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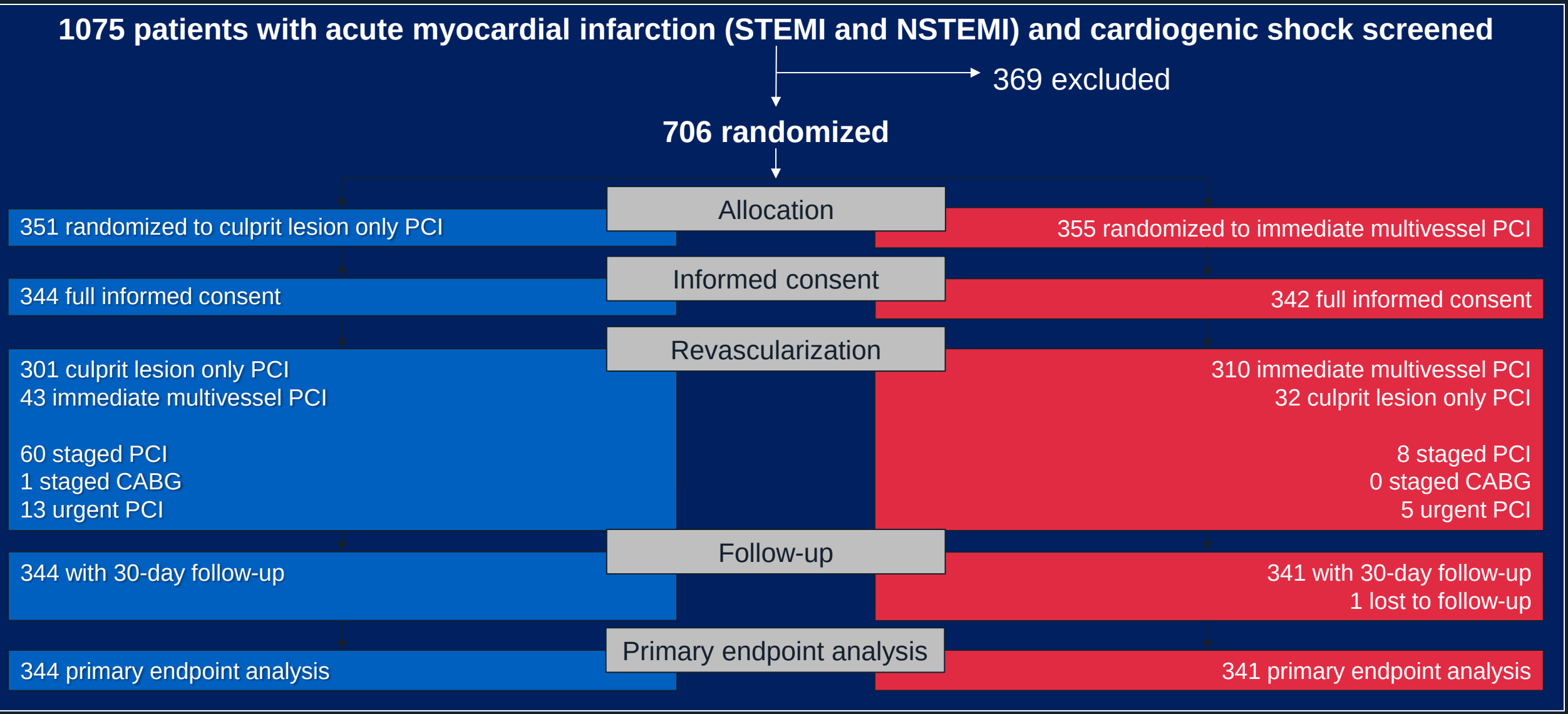
CULPRIT-SHOCK: Patients Disposition



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Thiele H, et al. N Engl J Med. 2017;377:2419-2432

CULPRIT-SHOCK: Baseline Characteristics

Characteristic	Culprit only PCI (n=344)	Multivessel PCI (n=342)
Age (years); median (IQR)	70 (60-78)	70 (60-77)
Male sex; n/total (%)	257/343 (74.9)	267/342 (78.1)
Prior myocardial infarction; n/total (%)	60/339 (17.7)	53/335 (15.8)
Prior PCI; n/total (%)	64/339 (18.9)	63/335 (18.8)
Prior coronary arterial bypass surgery; n/total (%)	20/341 (5.9)	13/337 (3.9)
Signs of impaired organ perfusion; n/total (%)		
Altered mental status	237/341 (69.5)	224/341 (65.7)
Cold, clammy skin and extremities	233/338 (68.9)	236/335 (70.4)
Oliguria	80/334 (24.0)	93/326 (28.5)
Arterial lactate >2.0 mmol/l	216/334 (64.7)	224/330 (67.9)
Fibrinolysis <24 h before randomization; n/total (%)	19/341 (5.6)	15/341 (4.4)
Resuscitation before randomization; n/total (%)	177/341 (51.9)	189/342 (55.3)
ST-elevation myocardial infarction; n/total (%)	206/335 (61.5)	209/330 (63.3)
No. of diseased vessels; n/total (%)		
1	3/343 (0.9)	2/342 (0.6)
2	122/343 (35.6)	124/342 (36.3)
3	218/343 (63.6)	216/342 (63.2)
Patients with at least one CTO; n/total (%)	77/344 (22.4)	82/342 (24.0)
Left ventricular ejection fraction (%); median (IQR)	33 (25-40)	30 (21-40)

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CULPRIT-SHOCK: Treatment

Characteristic	Culprit only PCI (n=344)	Multivessel PCI (n=342)	P value
Femoral access; n/total (%)	287/343 (83.7)	277/342 (81.0)	0.36
Radial access; n/total (%)	61/343 (17.8)	66/342 (19.3)	0.61
Stent implanted in culprit lesion; n/total (%)	326/343 (95.0)	324/342 (94.7)	0.86
Drug-eluting stent in culprit lesion; n/total (%)	305/326 (93.6)	308/324 (95.1)	0.41
TIMI-flow III post PCI of culprit lesion; n/total (%)	289/342 (84.5)	293/338 (86.7)	0.46
Immediate PCI of non-culprit lesions; n/total (%)	43/344 (12.5)	310/342 (90.6)	**<0.001**
Immediate complete revascularization; n/total (%)	26/344 (7.6)	277/342 (81.2)	**<0.001**
Total amount of contrast agent (ml); median (IQR)	190 (140-250)	250 (200-350)	**<0.001**
Staged PCI of non-culprit lesions; n/total (%)	60/344 (17.4)	8/341 (2.3)	**<0.001**
Staged coronary artery bypass surgery; n/total (%)	1/344 (0.3)	0/341	>0.99
Mechanical circulatory support; n/total (%)	99/344 (28.8)	95/342 (27.8)	0.77
Intraaortic balloon pump; n/total (%)	25/99 (25.3)	26/95 (27.4)	0.74
Impella 2.5; n/total (%)	16/99 (16.2)	18/95 (18.9)	0.61
Impella CP; n/total (%)	30/99 (30.3)	18/95 (18.9)	0.07
TandemHeart; n/total (%)	2/99 (2.0)	0/95	0.50
ECMO; n/total (%)	18/99 (18.2)	27/95 (28.4)	0.09
Mild hypothermia; n/total (%)	111/344 (32.3)	118/340 (34.7)	0.50
Mechanical ventilation; n/total (%)	273/344 (79.4)	282/339 (83.2)	0.20
Duration of mechanical ventilation (days); median (IQR)	3 (1-7)	3 (1-7)	0.97
Duration of intensive care treatment (days); median (IQR)	5 (2-12)	5 (2-11)	0.61

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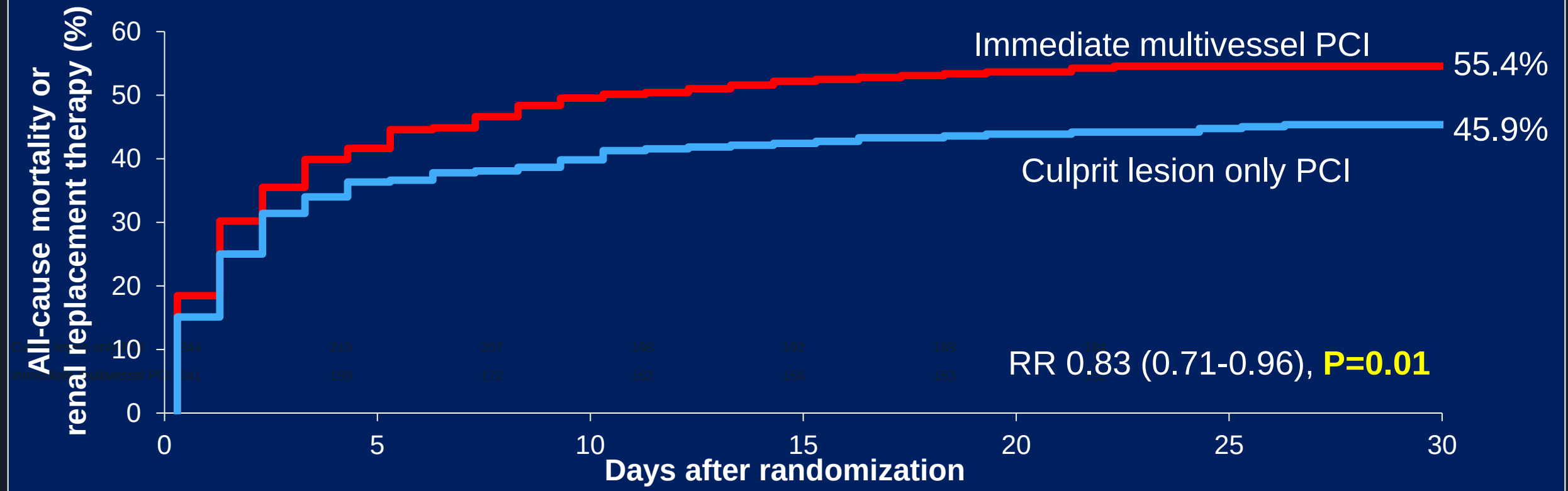
CULPRIT-SHOCK: Primary Endpoint

706 patients with MVD, AMI, and cardiogenic shock randomized to either PCI of the culprit lesion only or immediate multivessel PCI

All-cause mortality or renal replacement therapy at 30 days



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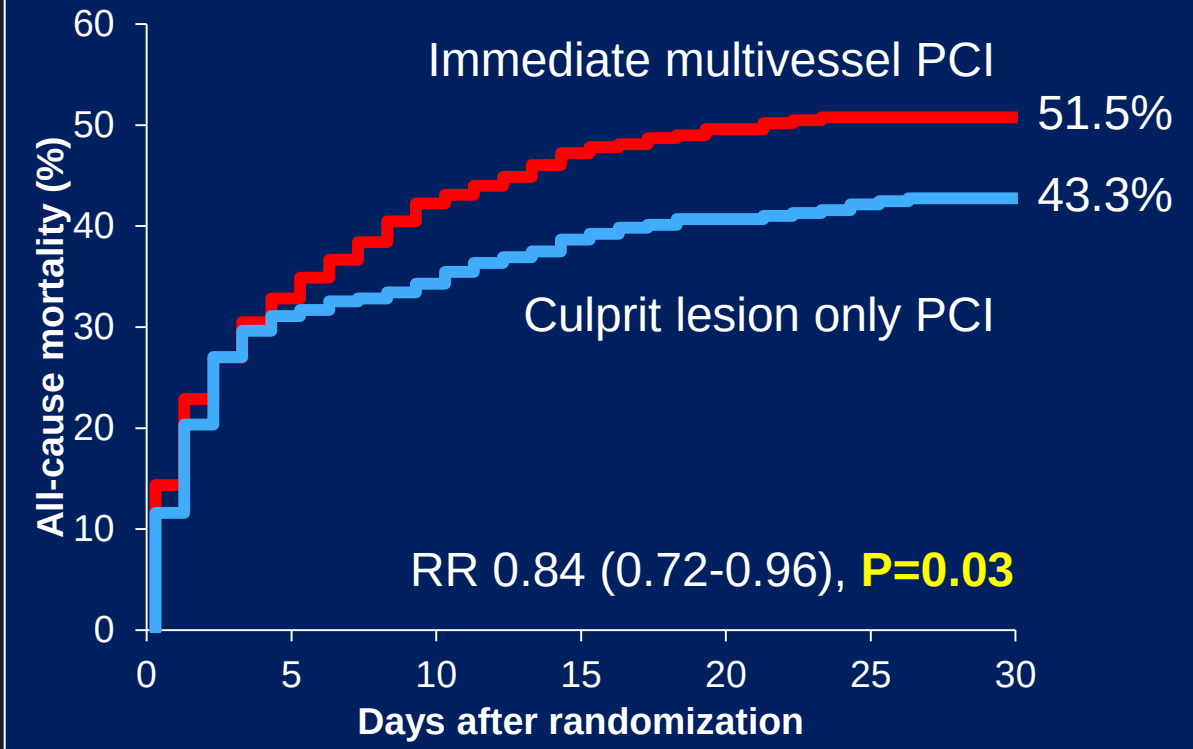
Thiele H, et al. N Engl J Med. 2017;377:2419-2432

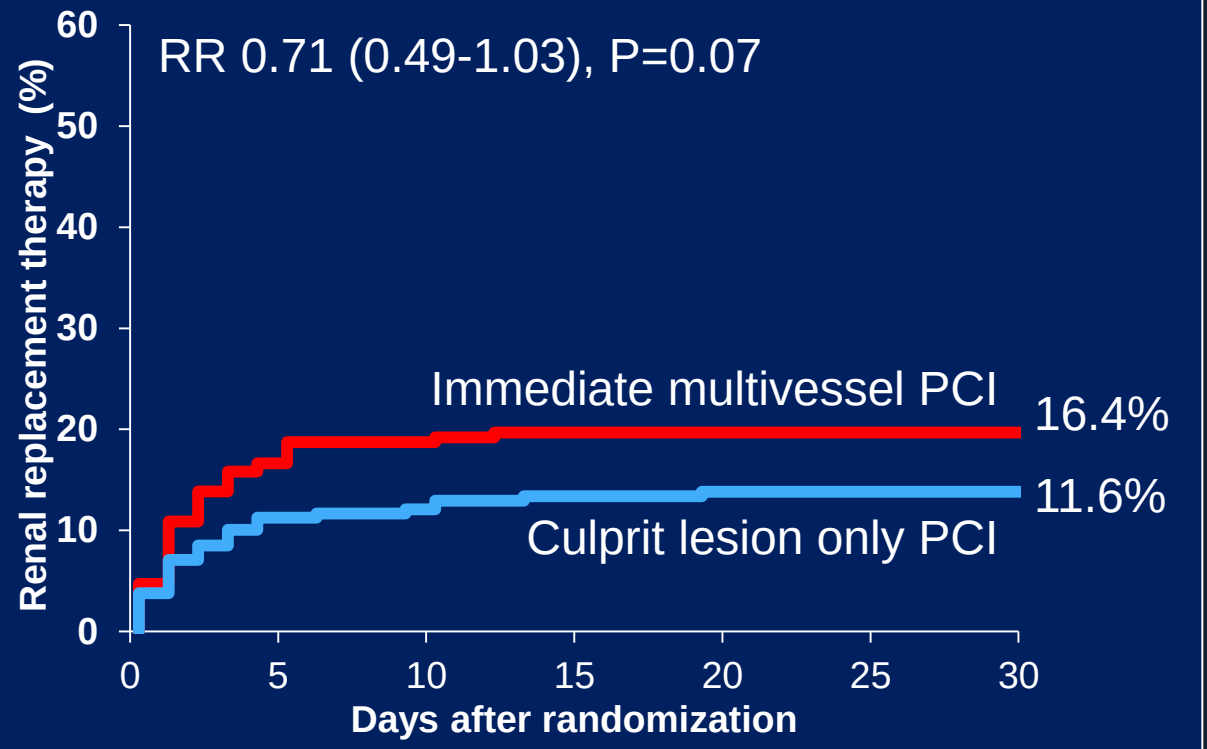
CULPRIT-SHOCK: Secondary Outcomes

706 patients with MVD, AMI, and cardiogenic shock randomized to either PCI of the culprit lesion only or immediate multivessel PCI

All-cause mortality



Renal replacement therapy



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CULPRIT-SHOCK: Other Secondary Outcomes

706 patients with MVD, AMI, and cardiogenic shock randomized to either PCI of the culprit lesion only or immediate multivessel PCI

Outcome	Culprit-Lesion-Only PCI Group (N = 344)	Multivessel PCI Group (N = 341)	P Value
Recurrent myocardial infarction	1.2%	0.9%	1.00
Rehospitalization for congestive heart failure	0.3%	0.3%	0.99
Death, recurrent myocardial infarction, or rehospitalization for congestive heart failure	43.9%	52.3%	**0.03**
Staged or urgent repeat revascularization	21.5%	3.8%	**<0.001**
Stroke	3.5%	2.9%	0.68
BARC type 2, 3, or 5 bleeding	16.6%	22.0%	0.07

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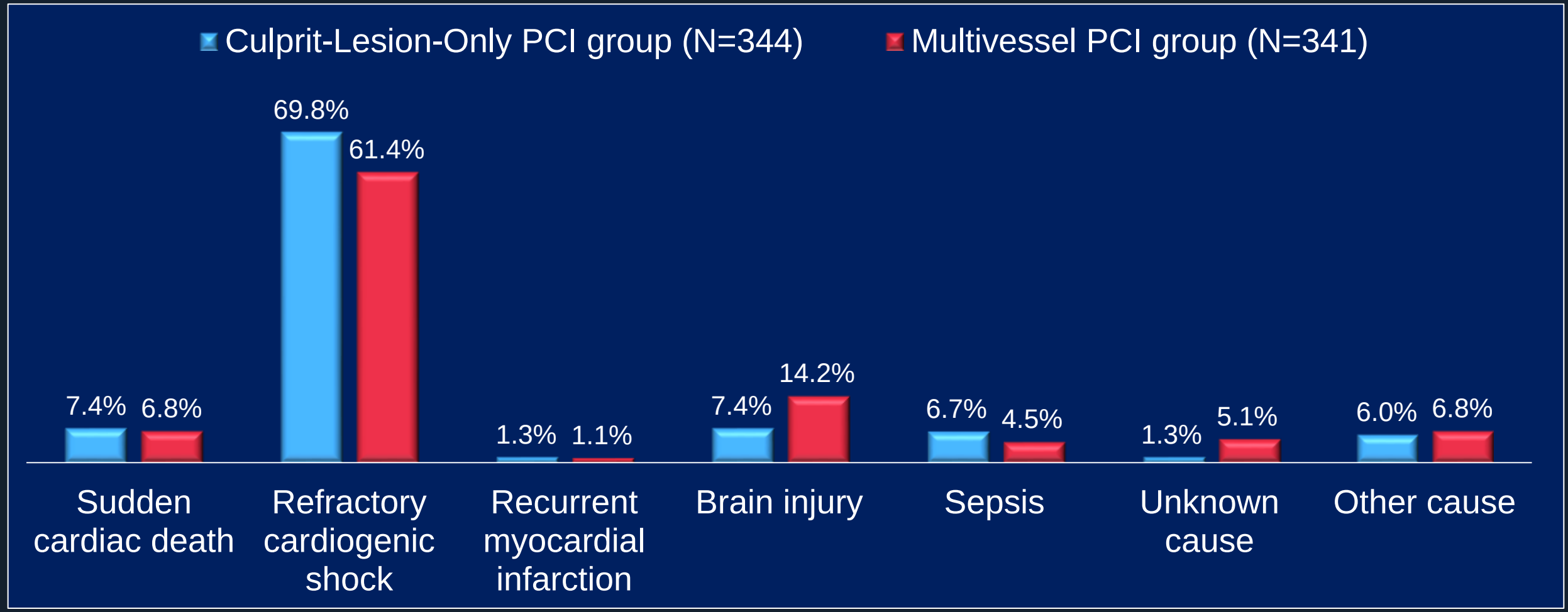
CULPRIT-SHOCK: Causes of Death

706 patients with MVD, AMI, and cardiogenic shock randomized to either PCI of the culprit lesion only or immediate multivessel PCI



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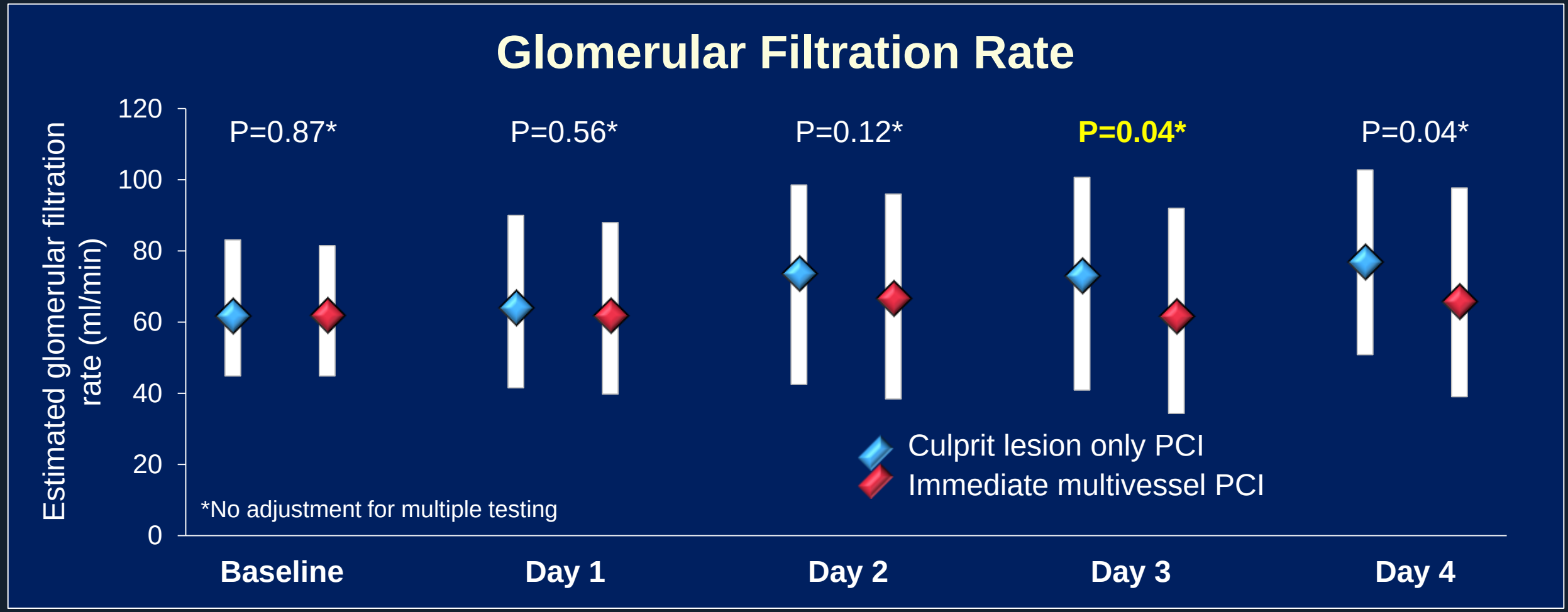
Thiele H, et al. N Engl J Med. 2017;377:2419-2432 (Online Appendix)

CULPRIT-SHOCK: Glomerular Filtration Rate

706 patients with MVD, AMI, and cardiogenic shock randomized to either PCI of the culprit lesion only or immediate multivessel PCI



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Was There an Influence of CTOs on Outcomes?

- CTO presence was not defined as an exclusion criterion in CULPRIT-SHOCK, because exclusion of CTO would have led to a major selection bias and a lower-risk cohort.
  - It was recommended to intervene on the CTO as easily as possible, with a limit of contrast agent of 300 cm^3 for the overall immediate multivessel PCI procedure and no retrograde or other complex interventional approaches were recommended.
  - At least 1 CTO was present in 22.4% in the culprit-lesion-only arm and in 24.0% in the immediate multivessel PCI arm. Immediate CTO recanalization was attempted in roughly 50% of patients in the immediate multivessel PCI group and was successful in approximately one third of attempts.

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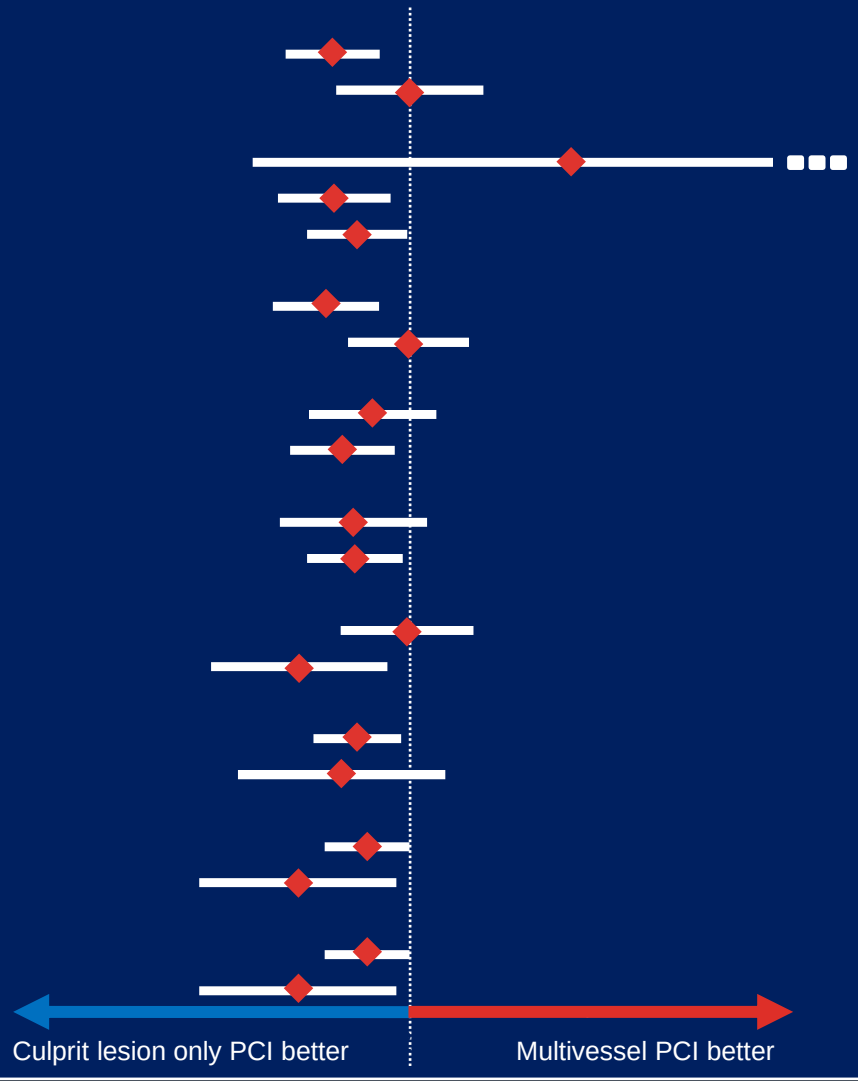
Thiele H, Desch S. Circulation. 2018;137:1314-1316

CULPRIT-SHOCK: Subgroups Analysis

Baseline Variable	Multivessel PCI	Culprit lesion only PCI	Relative Risk (95% CI)	P Value for Interaction
Sex				
Male	148/266 (55.6)	109/257 (42.4)	0.76 (0.64-0.91)	**0.11**
Female	41/75 (54.7)	48/86 (55.8)	1.02 (0.77-1.35)	
Age				
<50 years	3/16 (18.8)	6/17 (35.3)	1.88 (0.56-6.29)	**0.24**
50-75 years	114/226 (50.4)	82/212 (38.7)	0.77 (0.62-0.95)	
>75 years	72/99 (72.7)	70/115 (60.1)	0.84 (0.69-1.01)	
Diabetes				
No	116/218 (53.2)	93/235 (39.6)	0.74 (0.61-0.91)	**0.08**
Yes	66/116 (56.9)	59/102 (57.8)	1.02 (0.81-1.28)	
Hypertension				
No	68/129 (52.7)	65/139 (46.8)	0.89 (0.70-1.13)	**0.47**
Yes	114/205 (55.6)	88/200 (44.0)	0.79 (0.65-0.97)	
Type of infarction				
NSTEMI	54/97 (55.7)	45/98 (45.9)	0.82 (0.62-1.09)	**0.96**
STEMI	128/233 (54.9)	108/237 (45.6)	0.83 (0.69-0.99)	
STEMI type				
Anterior infarction	59/113 (52.2)	57/108 (52.8)	1.01 (0.79-1.30)	**0.07**
Non-anterior infarction	48/92 (52.2)	34/97 (35.0)	0.67 (0.48-0.94)	
Previous infarction				
No	154/281 (54.8)	128/279 (45.9)	0.84 (0.71-0.99)	**0.83**
Yes	28/53 (52.8)	25/60 (41.7)	0.79 (0.53-1.17)	
Coronary artery disease				
2-vessel disease	64/124 (51.6)	48/122 (39.3)	0.76 (0.58-1.01)	**0.56**
3-vessel disease	124/215 (57.7)	109/218 (50.0)	0.87 (0.73-1.03)	
Chronic total occlusion				
No	146/259 (56.4)	131/267 (49.1)	0.87 (0.74-1.02)	**0.26**
Yes	43/82 (52.4)	27/77 (35.1)	0.67 (0.46-0.97)	



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A "Real World" Series of Cardiogenic Shock

KAMIR-NIH registry: 659 pts who underwent multivessel PCI (39.5%) or infarct-related artery (IRA)-only PCI (60.5%) between Nov 2011 and Dec 2015

Outcome	Multivessel PCI (N = 260)	IRA-only PCI (N = 399)	Adjusted HR (95% CI)	P value
All-cause death	21.3%	31.7%	0.52 (0.38–0.73)	**<0.001**
Cardiac death	17.4%	27.5%	0.53 (0.37–0.77)	**0.001**
Recurrent MI	2.2%	3.3%	0.65 (0.20–2.09)	0.47
Any revascularization	11.6%	16.5%	0.50 (0.27–0.93)	**0.027**
Non-IRA revascularization	6.7%	8.2%	0.33 (0.14–0.78)	**0.011**
Definite or probable ST	1.4%	1.4%	0.53 (0.04–7.89)	0.65
Death or MI	22.4%	33.9%	0.57 (0.42–0.79	**0.001**
Death or new RRT	21.3%	32.6%	0.52 (0.37–0.72)	**<0.001**
POCE	28.4%	42.6%	0.58 (0.40–0.83)	**0.003**

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Lee JM, et al. J Am Coll Cardiol. 2018;71:844-856

How Can We Solve this Discrepancy?

	CULPRIT-SHOCK	KAMIR-NIH
Type	RCT	Registry
Patients	706	659
30-day mortality	47.4%	21.9%
Mechanical circulatory support	28%	27%
IRA-only PCI	50%	60.6%
Multivessel PCI	50%	39.4%
Immediate multivessel PCI	90.6%	60.4%
Staged non-IRA PCI	2.3%	39.6%
Complete revascularization	81% (immediate)	65.8%
CTO	24%	NR
CTO-PCI	~12%	NR
CTO-PCI success	~4%	NR

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Recommendations for Multivessel PCI With Acute Myocardial Infarction and Cardiogenic Shock

Current Recommendation (2017)	Class	LOE
Non-IRA PCI during the index procedure should be considered in patients with cardiogenic shock.	IIa	C

Potential Update (?)	Class	LOE
PCI limited to the culprit lesion is recommended on a routine basis with an option for staged revascularization.	I	A or B
Routine immediate multivessel PCI is not recommended in patients with cardiogenic shock.	III	B

- CULPRIT-SHOCK

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Thiele H, Desch S. Circulation. 2018;137:1314-1316

Closing Remarks

- Based on CULPRIT-SHOCK, culprit-lesion-only PCI with possible staged revascularization should be the preferred revascularization strategy, which can also be translated as “keep the revascularization strategy simple.”
- However, areas of uncertainty remain:
  1. What are the underlying mechanisms for the observed difference in mortality?
  2. Would complete revascularization by CABG make a difference?
  3. What is the optimal timing for staged revascularization in cardiogenic shock patients?
  4. Any difference in outcomes with timely initiation of powerful mechanical circulatory support?

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