National Institute for Health Research, Leicester
Cardiovascular Biomedical Research Unit

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Multi-vessel disease in CGS

A case-based discussion

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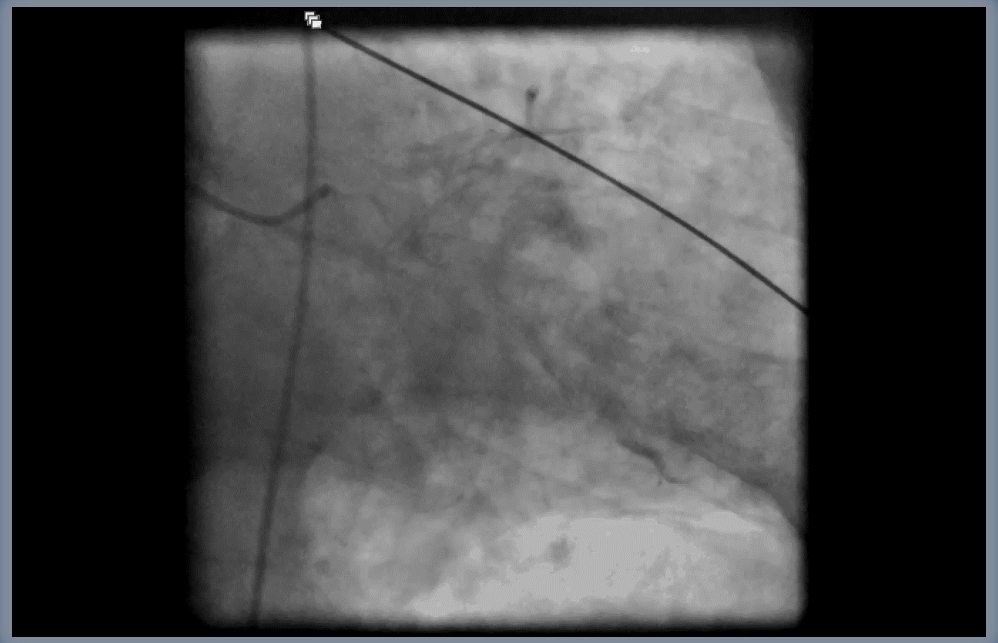
CGS happens when significant myocardium is at risk



Salvaging

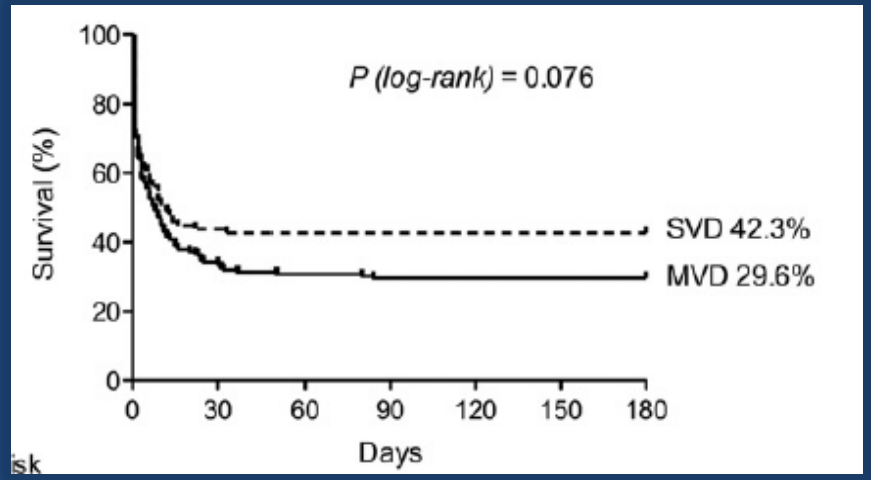
The physiological hypothesis is that complete myocardial revascularisation, reduces overall ischaemia and so myocardial perfusion improves with consequent improvement in acute haemodynamics and LV systolic function, hence stopping the spiral of decline that occurs in cardiogenic shock.

In patients presenting with CGS ：

1. Incidence MVD in CGS patients

SHOCK trial	60%	*Hochman JS N Engl J Med 1999 341 625-*
NCDR CathPCI Registry	63%	*Mehta RH JACC CV Interv 2009 2 56-*
EHS-PCI Registry	*64%*	*Bauer TAm J Cardiol. 2012;109(7):941-*

2. CGS plus MVD do worse



Survival to 6 months in patients with

single-vessel (SVD) or multivessel (MVD)

Mylotte J Am Coll Cardiol Intv 2013;6:115

Size of infarct

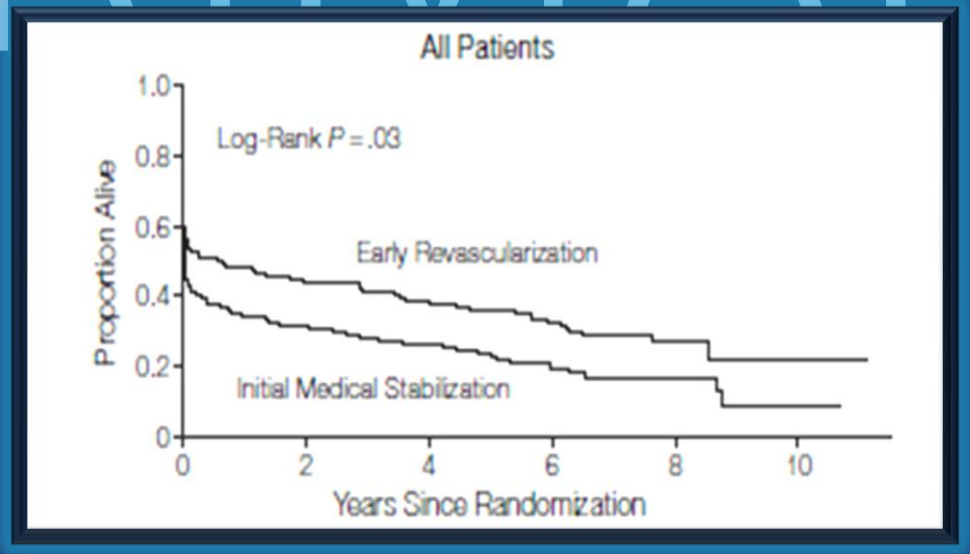
Revascularisation : The data

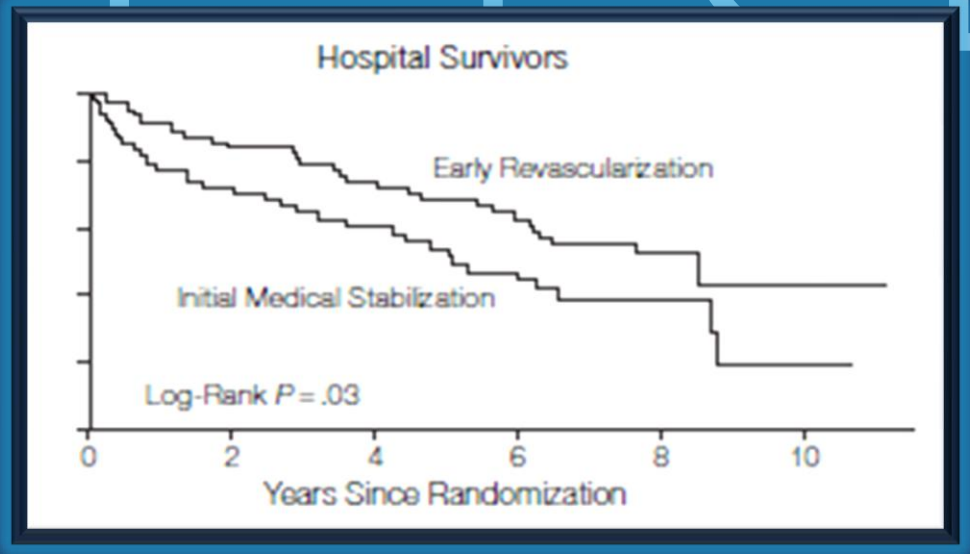
Early Revascularization and Long-term Survival in Cardiogenic Shock Complicating Acute Myocardial Infarction

PRIMARY PCI

SHOCK Trial

302 patients 1993 -1998

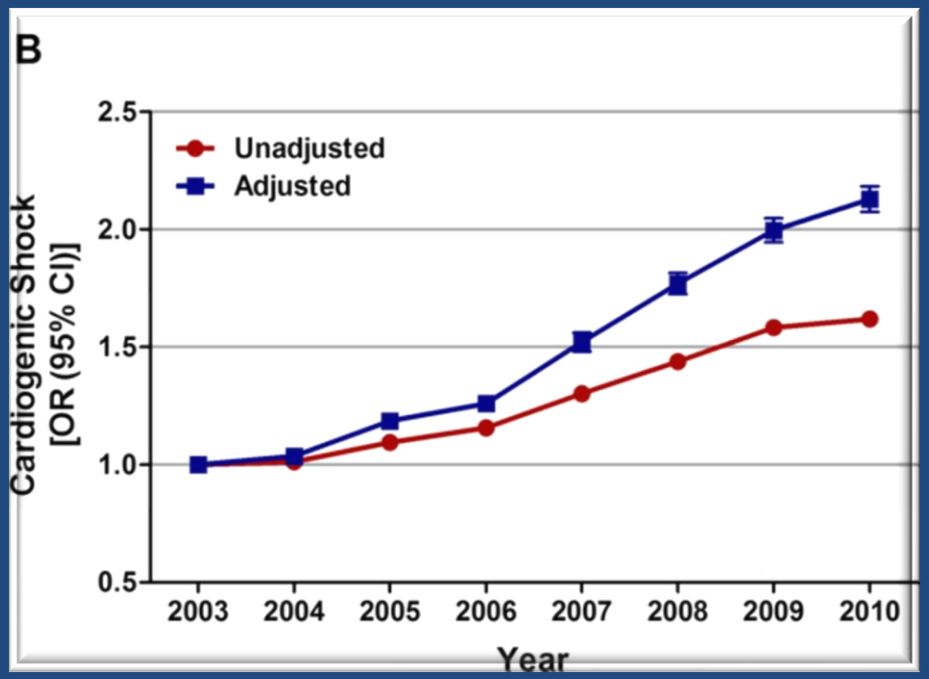




Recommendations	Class [a]	Level [b]	Ref [c]
In all patients with suspected cardiogenic shock, immediate ECG and echocardiography are recommended.	I	C	
All patients with cardiogenic shock should be rapidly transferred to a tertiary care center which has a 24/7 service of cardiac catheterization, and a dedicated ICU/CCU with availability of short-term mechanical circulatory support.	I	C	
In patients with cardiogenic shock complicating ACS an immediate coronary angiography is recommended (within 2 hours from hospital admission) with an intent to perform coronary revascularization.	I	C	
Continous ECG and blood pressure monitoring are recommended.	I	C	
Invasive monitoring with an arterial line is recommended.	I	C	
Fluid challenge (saline or Ringer's lactate, >200 ml/15–30 min) is recommended as the first-line treatment if there is no sign of overt fluid overload.	I	C	
Intravenous inotropic agents (dobutamine) may be considered to increase cardiac output.	IIb	C	
Vasopressors (norepinephrine preferable over dopamine) may be considered if there is a need to maintain SBP in the presence of persistent hypoperfusion.	IIb	B	558
IABP is not routinely recommended in cardiogenic shock.	III	B	585, 586
Short-term mechanical circulatory support may be considered in refractory cardiogenic shock depending on patient age, comorbidities and neurological function.	IIb	C	

But

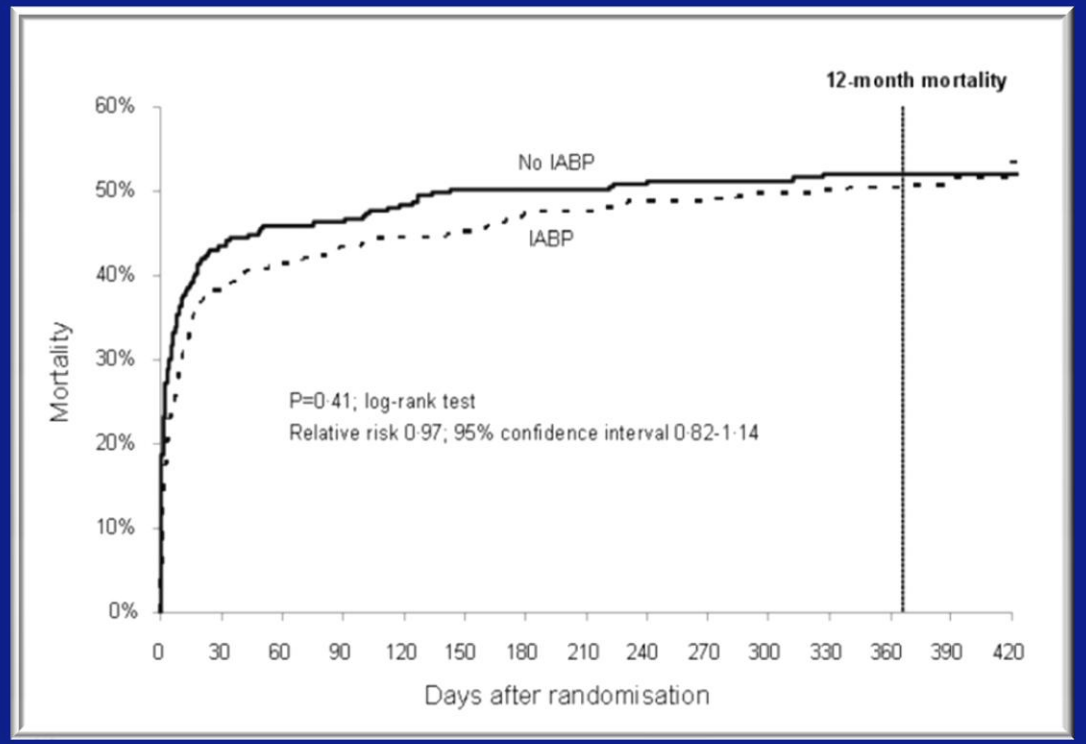
- Adjusted rates show two-fold increase in cardiogenic shock from 2003 to 2010.



Kolte D et al. JAHA 2014; 3: e000590

- Earlier diagnosis and treatment
- New Pharma
- MSD
- Both
- Rx MVD

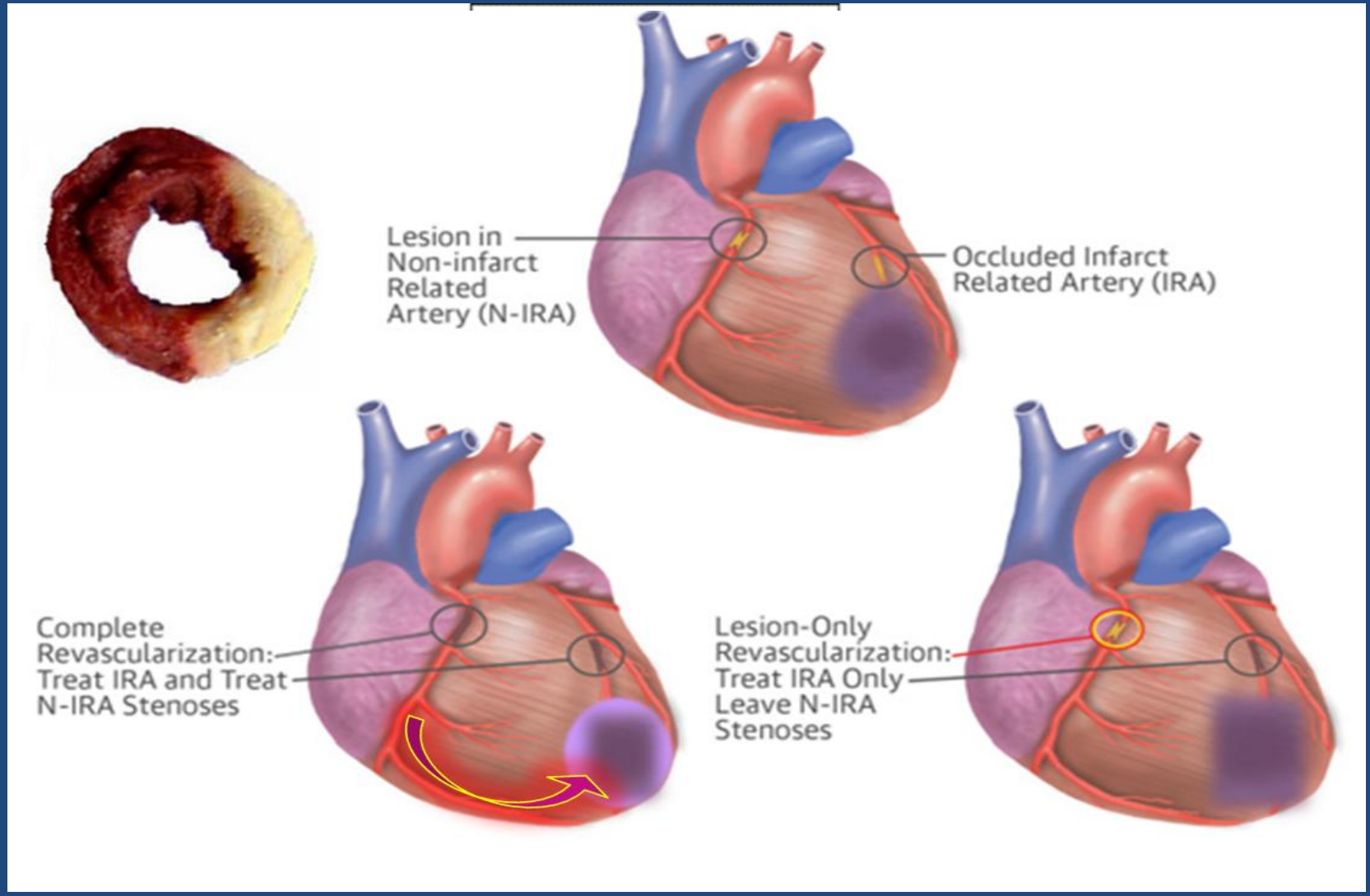
- Mortality remains at about 50% .



Thiele H et al Lancet 2013;382:1638–1645

Pros and Cons of treating MVD (STEMI/CGS)

Advantages	Disadvantages
Patients with MVD do worse	Increased contrast load → risk of contrast-induced nephropathy
Treatment of remote ischemia	Radiation exposure
	Complications of treating additional lesions so called “double jepody ”
Reduced subsequent hospitalization for the patients and with resultant economic benefits	Coronary spasm might overestimate stenosis severity of non-culprit stenoses Is it severe ???
Reduction in vascular complications by having all PCI performed during the index intervention through a single access site	Additional revascularization may not reduce ischemia >intensive medical therapy
Patient preference/comfort	Increased risk of early/late stent thrombosis
Improved hemodynamics	Hemodynamic instability might be worsened by treating additional lesions
Limit infarct size and preserve left ventricular ejection fraction	



Complete revascularisation can be regarded as an important factor by restoring blood flow to recoverable myocardium so slowing the progressive vicious cycle that ultimately leads to coronary and systemic hypoperfusion and death.

Management of Multivessel Disease and Cardiogenic Shock

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Table 1
Summary of studies comparing culprit-only and multivessel PCI in cardiogenic shock

Study	Description	Outcomes
NO BENEFIT MVD REVASCULAIZATION		
Bauer et al,[25] 2012	Retrospective analysis of 336 patients	No significant difference in in-hospital
WORSE OUTCOME MVD REVASCULAIZATION		
Cavender et al,[23] 2009	Retrospective analysis of 3134 patien MVD NCDR patien cardio whom (14%)	Significantly higher in-hospital
Van Der Schaff et al,[24] 2010		
Zeymer et al,[7] 2015	Prospect registr with c MVD; this co time c	
Yang et al,[26] 2014		
IMPROVED OUTCOME MVD REVASCULAIZATION		
Mylotte et al,[27] 2013	Multicenter prospective observational study of STEMI patients presenting with cardiogenic shock and resuscitated cardiac arrest; 266 patients, 97 patients (36.5%) with single vessel disease and 169 patients with MV disease. In MVD cohort, 66 (39.0%) of patients underwent MV-PCI.	6-mo survival significantly greater in MV-PCI group compared with culprit-only PCI in MVD (43.9% vs 20.4%, $P = .0017$). MV-PCI at time of PPCI was an independent predictor of 6-mo survival (HR = 0.57, 95% CI = 0.38–0.84, $P = .005$)
Hussein et al,[8] 2011	210 cardiogenic shock patients, of whom 101 patients underwent MV-PCI; 17% of the PCI cohort underwent MV-PCI	Survival to discharge higher in MV-PCI group (76% vs 44% in culprit-only group, $P<.001$). Complete revascularization was an independent predictor of survival to discharge (OR = 6.2, 95% CI = 1.85–24.6, $P = .005$)
Park et al,[28] 2015	Retrospective analysis of 1105 patients with STEMI and cardiogenic shock; 510 patients had MVD; culprit-only revascularization in 386 patients, MV-PCI at time of index PCI in 124	In-hospital mortality lower in MV-PCI group (2.4% vs 9.3% for culprit-only PCI)

Intervent Cardiol Clin ■ (2016) ■–■
http://dx.doi.org/10.1016/j.iccl.2016.06.009

Manitoba cardiogenic SHOCK registry

210 consecutive patients analysed for independent predictors of in-hospital mortality

Following multivariate logistic regression achieving complete revascularisation either with PCI or CABG was an independent predictor of survival to discharge (OR=2.5, 95%CI=1.1-6.2, p=0.025)

The Euro-Heart Survey-PCI registry

increased tendency towards in-hospital mortality with MV-PCI

(48.8% vs 37.4% for culprit-only PCI, p=0.07), but sicker patients requiring ventilation were more likely to undergo multivessel PCI (30% vs 19%, p=0.05).

- Correcting for confounders using multivariate logistic regression analysis attenuated this difference in in-hospital mortality between the 2 groups (OR=1.28, 95%CI=0.72-2.28) (33).

Culprit or multivessel revascularisation in ST-elevation myocardial infarction with cardiogenic shock

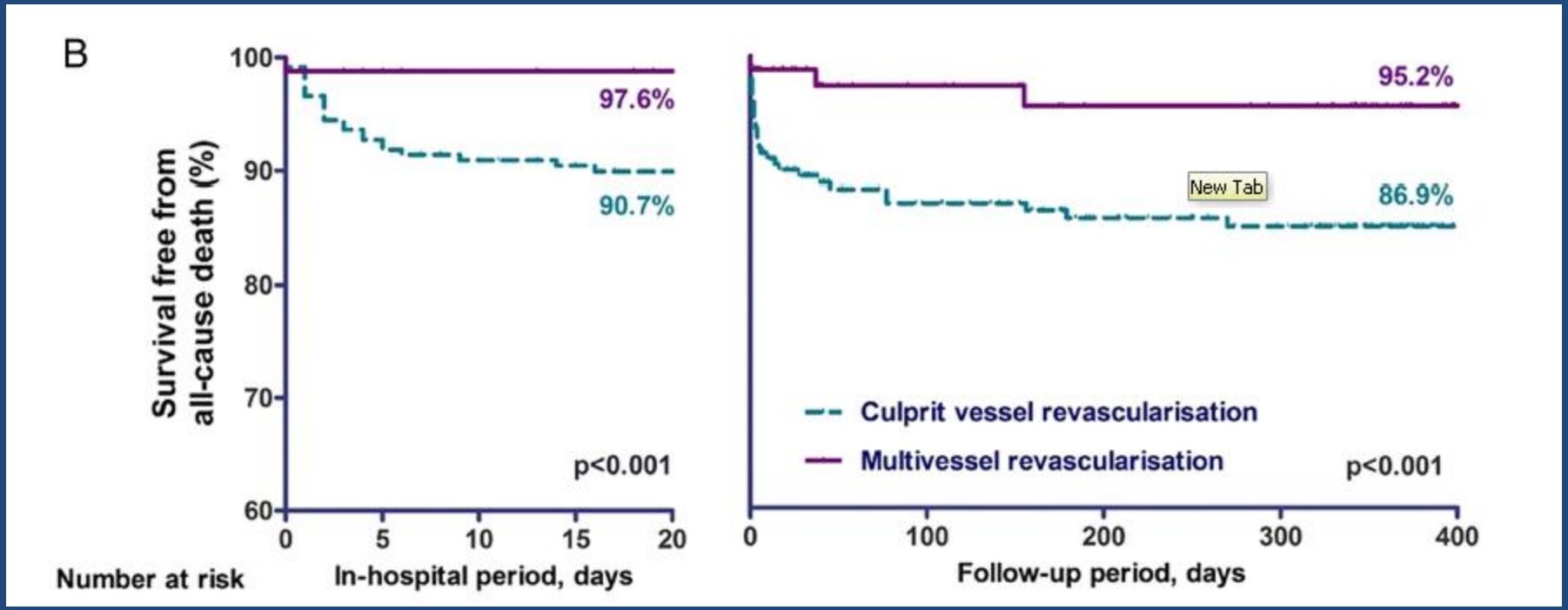
Jin Sup Park,[1] Kwang Soo Cha,[1,2] Dae Sung Lee,[1] Donghun Shin,[1] Hye Won Lee,[1] Jun-Hyok Oh,[1] Jeong Su Kim,[3] Jung Hyun Choi,[1] Yong Hyun Park,[3] Han Cheol Lee,[1] June Hong Kim,[3] Kook-Jin Chun,[3] Taek Jong Hong,[1] Myung Ho Jeong,[4] Youngkeun Ahn,[4] Shung Chull Chae,[5] Young Jo Kim,[6] the Korean Acute Myocardial Infarction Registry Investigators

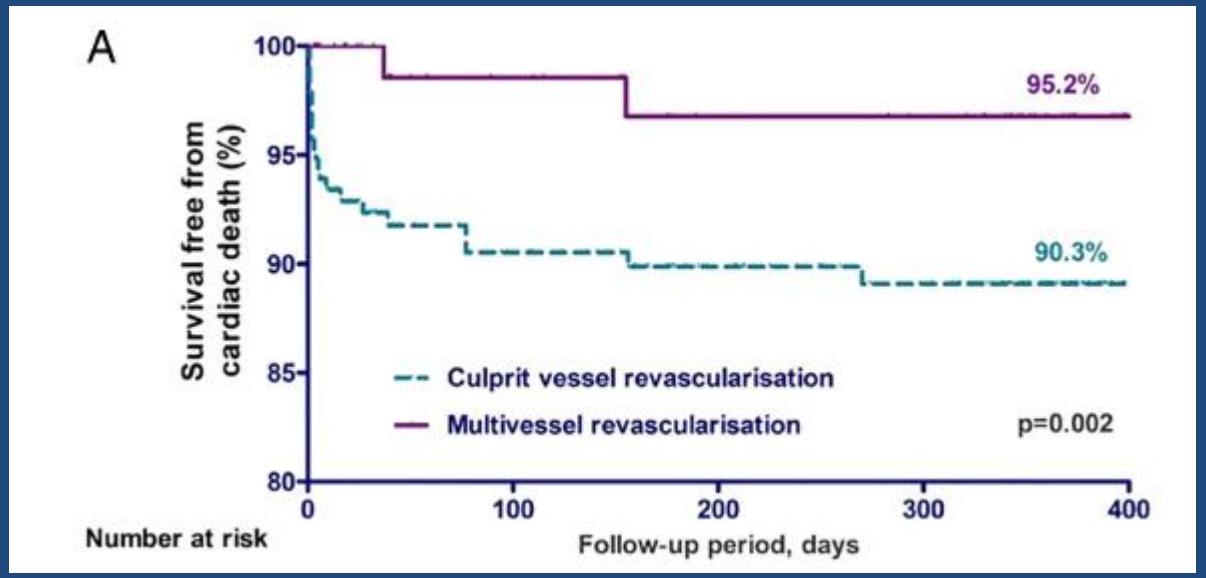
Heart. 2015 Aug;101(15):1225-32.

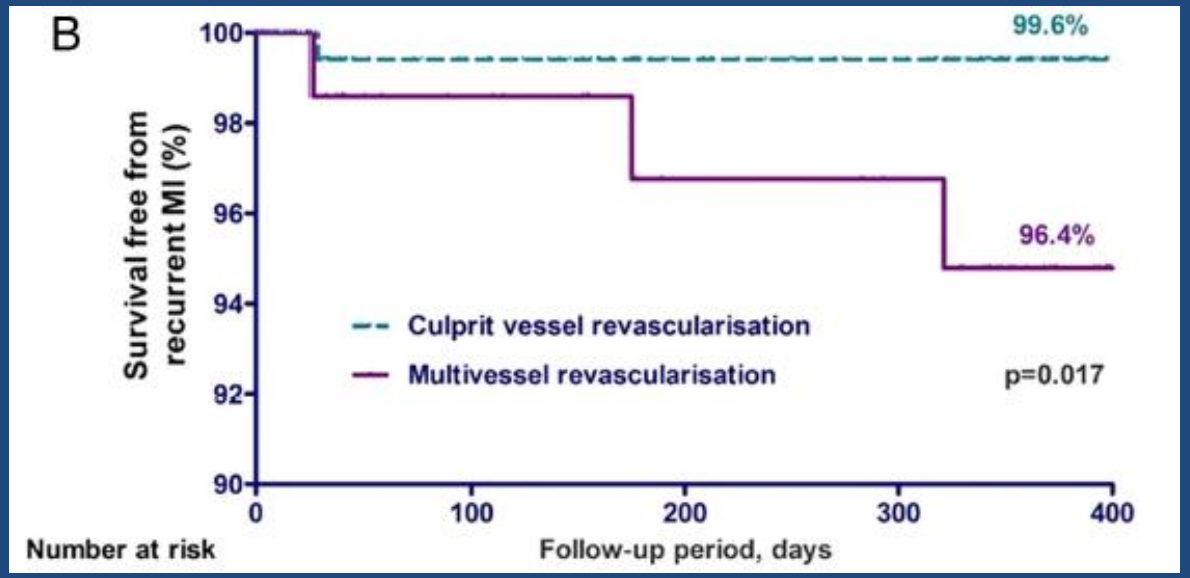
16 620 patients with STEMI prospective, multicentre registry between January 2006 and December 2012, 510 eligible patients were selected and divided into

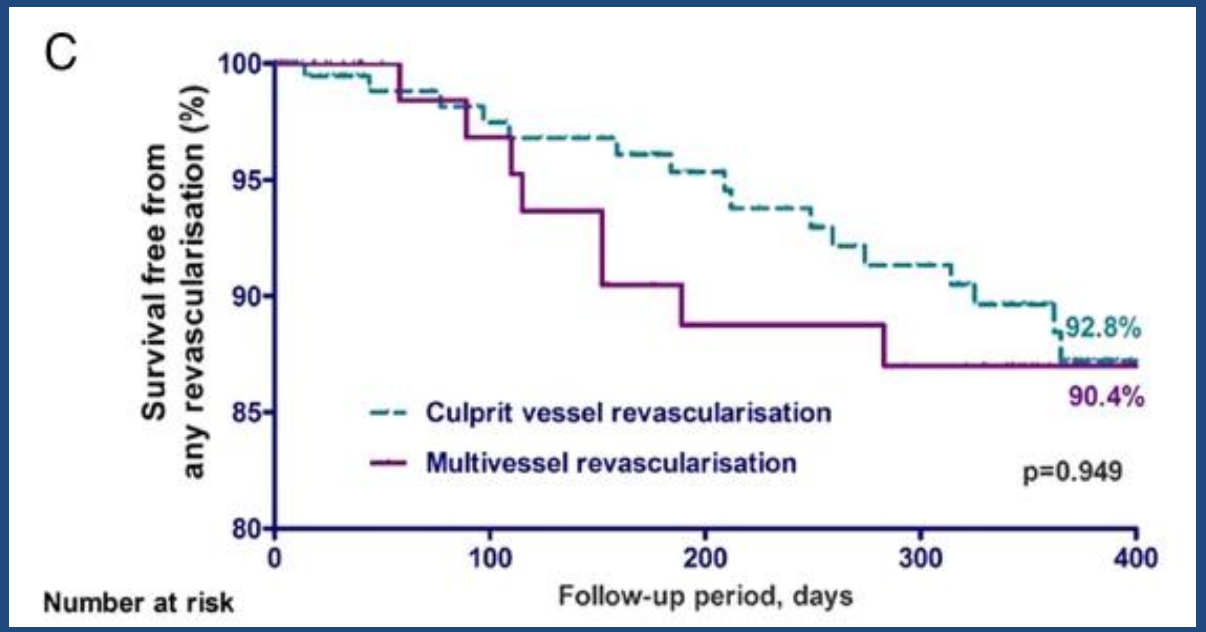
- culprit vessel revascularisation (n=386, 75.7%)
- multivessel revascularisation (n=124, 24.3%)

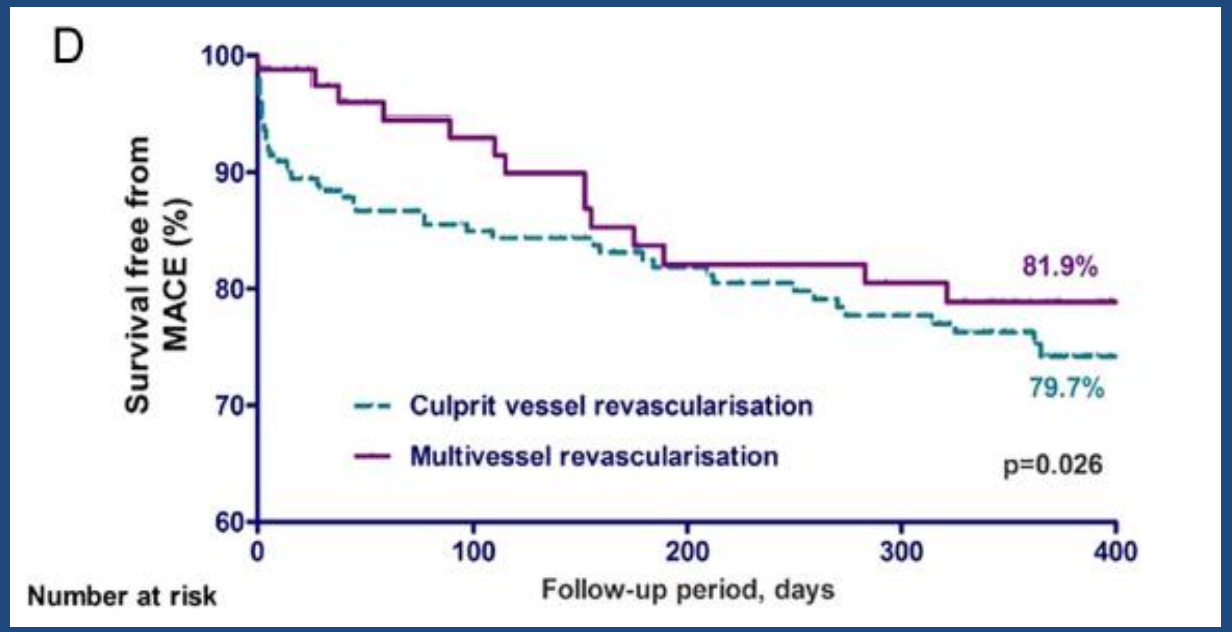
The primary outcomes were in- hospital mortality and all-cause death during a median 194-day follow-up


B
Survival free from all-cause death (%)
100
90
80
70
60
97.6%
90.7%
p<0.001
0
5
10
15
20
In-hospital period, days
Number at risk
95.2%
86.9%
New Tab
Culprit vessel revascularisation
Multivessel revascularisation
p<0.001
0
100
200
300
400
Follow-up period, days









Heart. 2015 Aug;101(15):1225-32.

Table 4 Predictors of inhospital mortality

	Simple Cox regression		Multiple Cox regression	
Variable	HR (95% CI)	p Value	HR (95% CI)	p Value
Age (1-year increase)	1.073 (1.049 to 1.098)	<0.001	1.064 (1.019 to 1.110)	0.005
Female sex	2.693 (1.676 to 4.328)	<0.001		
Cardiopulmonary resuscitation	4.165 (2.065 to 8.400)	<0.001		
Systolic blood pressure	0.993 (0.984 to 1.002)	0.108		
Overt pulmonary oedema	3.332 (1.981 to 5.603)	<0.001		
Ischaemic heart disease	0.515 (0.207 to 1.282)	0.154		
Hypertension	1.688 (1.010 to 2.822)	0.046		
Diabetes mellitus	1.722 (1.028 to 2.884)	0.039		
Dyslipidaemia	0.175 (0.024 to 1.270)	0.085		
Preprocedural TIMI flow grade 0–1	1.146 (0.844 to 1.556)	0.381		
Postprocedural TIMI flow grade 2–3	0.228 (0.136 to 0.384)	<0.001	0.242 (0.085 to 0.685)	0.008
Use of intra-aortic balloon pump	5.000 (3.116 to 8.023)	<0.001	3.286 (1.350 to 7.997)	0.009
Low left ventricular EF	0.918 (0.890 to.0948)	<0.001	0.938 (0.903 to 0.974)	0.001
Serum glucose level	1.006 (1.004 to 1.008)	<0.001		
Serum creatinine level	1.577 (1.372 to 1.813)	<0.001	1.816 (1.249 to 2.639)	0.002
Ventricular tachycardia/fibrillation*	3.636 (2.143 to 6.169)	<0.001		
Contrast-induced nephropathy*	8.391 (3.625 to 19.422)	<0.001	6.165 (1.977 to 19.222)	0.002
Major bleeding*	4.236 (1.037 to 17.297)	0.044		

Table 5 Predictors of all-cause death during follow-up

	Simple Cox regression		Multiple Cox regression	
Variable	HR (95% CI)	p Value	HR (95% CI)	p Value
Age (1-year increase)	1.071 (1.049 to 1.093)	<0.001	1.079 (1.040 to 1.120)	<0.001
Female sex	2.131 (1.392 to 3.261)	<0.001		
Cardiopulmonary resuscitation	3.445 (1.723 to 6.888)	<0.001		
Systolic blood pressure	0.994 (0.986 to 1.003)	0.182		
Overt pulmonary oedema	3.387 (2.124 to 5.401)	<0.001		
Ischaemic heart disease	0.859 (0.443 to 1.665)	0.653		
Hypertension	1.611 (1.019 to 2.547)	0.041		
Diabetes mellitus	1.632 (1.021 to 2.607)	0.041		
Dyslipidaemia	0.563 (0.205 to 1.545)	0.265		
Preprocedural TIMI flow 0–1	1.668 (0.905 to 3.077)	0.101		
Postprocedural TIMI flow 2–3	0.264 (0.162 to 0.428)	<0.001	0.336 (0.142 to 0.793)	0.013
Use of intra-aortic balloon pump	4.451 (2.891 to 6.853)	<0.001	2.531 (1.246 to 5.141)	0.010
Low left ventricular EF	0.932 (0.909 to 0.955)	<0.001	0.948 (0.921 to 0.976)	<0.001
Serum glucose level	1.005 (1.003 to 1.007)	<0.001		
Serum creatinine level	1.597 (1.403 to 1.819)	<0.001	1.784 (1.326 to 2.402)	<0.001
Ventricular tachycardia/fibrillation*	3.297 (2.010 to 5.407)	<0.001		
Contrast-induced nephropathy*	9.078 (4.167 to 19.778)	<0.001	5.928 (2.149 to 16.355)	0.001
Major bleeding*	3.699 (0.909 to 15.056)	0.068		

Conclusions

This study showed that multivessel compared with culprit vessel revascularisation during primary PCI was associated with better outcomes in patients with STEMI with cardiogenic shock and MVD, supporting current revascularisation guidelines.

The issue with patient selection in analyses in retrospective registries of this heterogeneous condition is also shown in the Korean Acute Myocardial Infarction Registry (KAMIR) registry of 31,149 patients with acute MI enrolled, which reviewed outcomes in 1,105 patients with STEMI and CGS. Of these patients, 510 had evidence of multivessel disease on angiography.

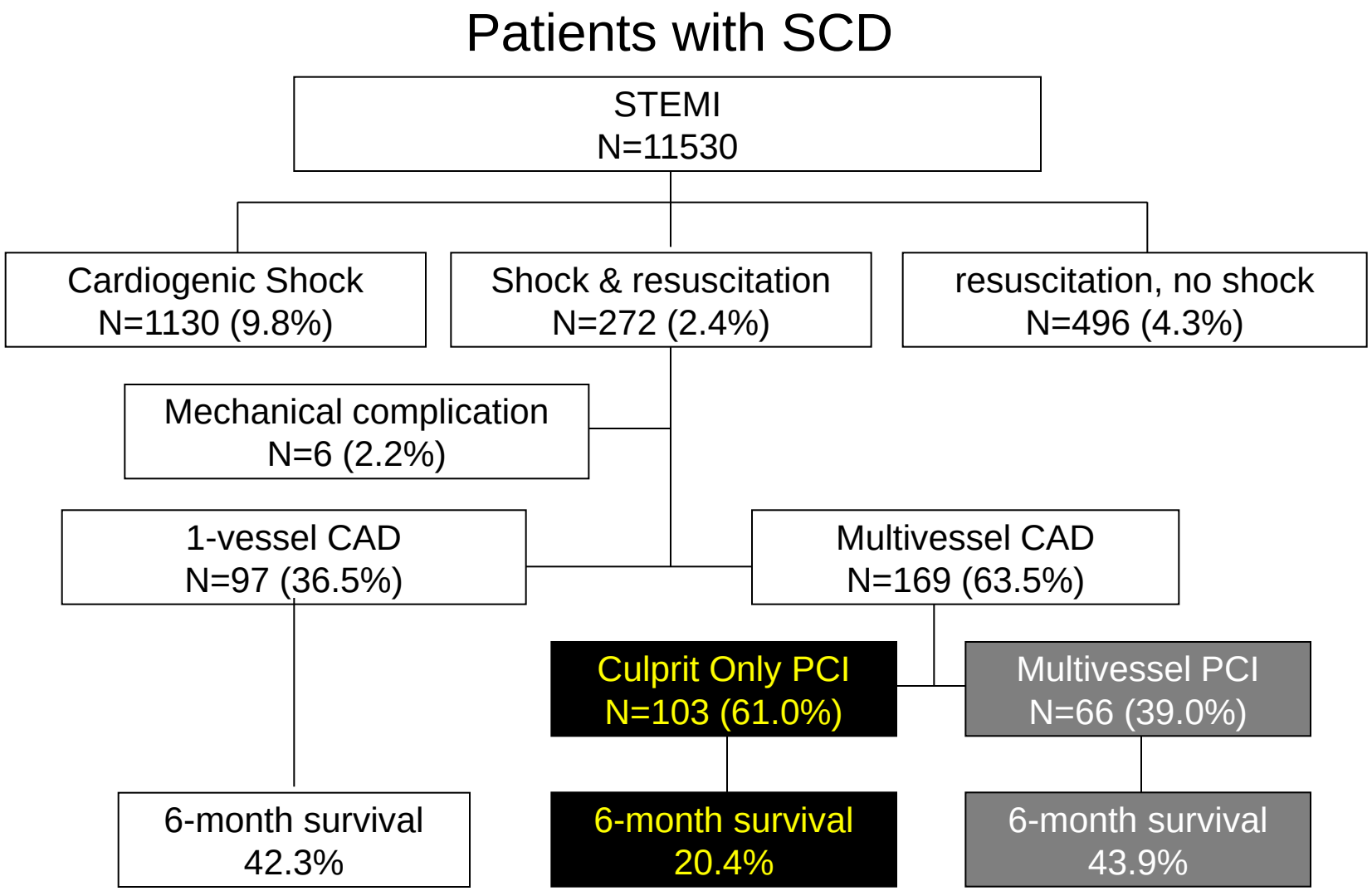
The mean LVEF in both groups was >50%, higher than would be expected in patients with multivessel disease and cardiogenic shock.

In spite of adjustment using cox proportional hazards models with inverse-probability weighting; there may have been specific risk factors that influence choice of one revascularisation strategy over another as with any observational retrospective study.

Mortality for multivessel vs. culprit lesion only PCI in cardiogenic shock in registries

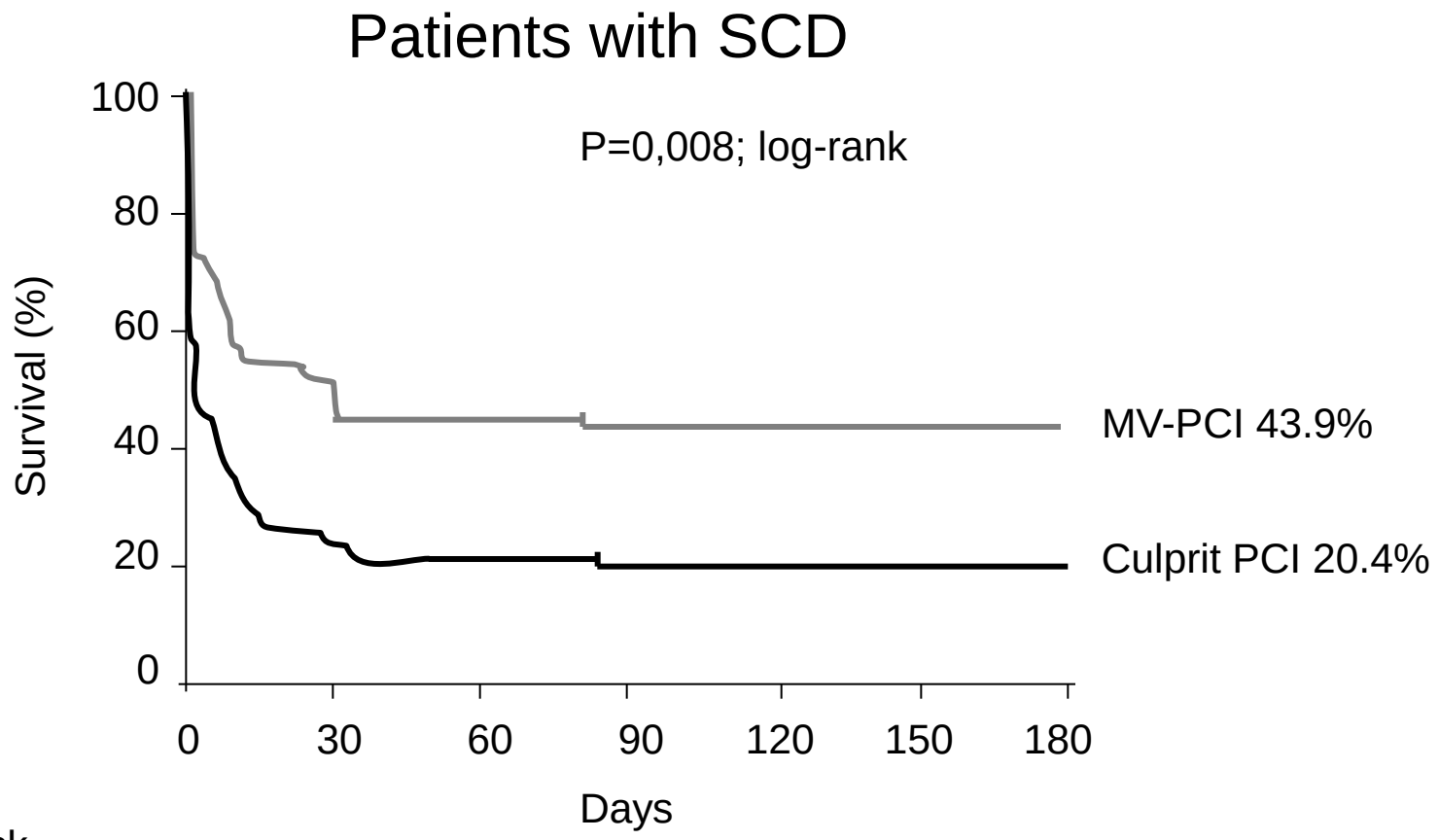
Trial	*N*	Mortality multivessel PCI, %	Mortality culprit lesion only PCI, %	Adjusted odds ratio or hazard ratio (95% CI)
Webb *et al.*[18]	74	55	20	2.75 (1.05–7.25)
Van der Schaaf *et al.*[22]	161	60	53	Not reported (*P* =0.05)
Cavender *et al.*[23]	3087	36.5	27.8	1.5 (1.22–1.95)
Bauer *et al.*[21]	336	48.8	37.4	1.28 (0.72–2.28)
Zeymer *et al.*[25]	735	46.8	35.8	1.5 (1.15–1.84)
Yang *et al.*[26]	338	35.0	30.6	1.06 (0.61–1.86)
Mylotte *et al.*[24]	266	20.4	43.9	0.57 (0.38–0.84)

Multivessel PCI or Culprit Lesion Only PCI



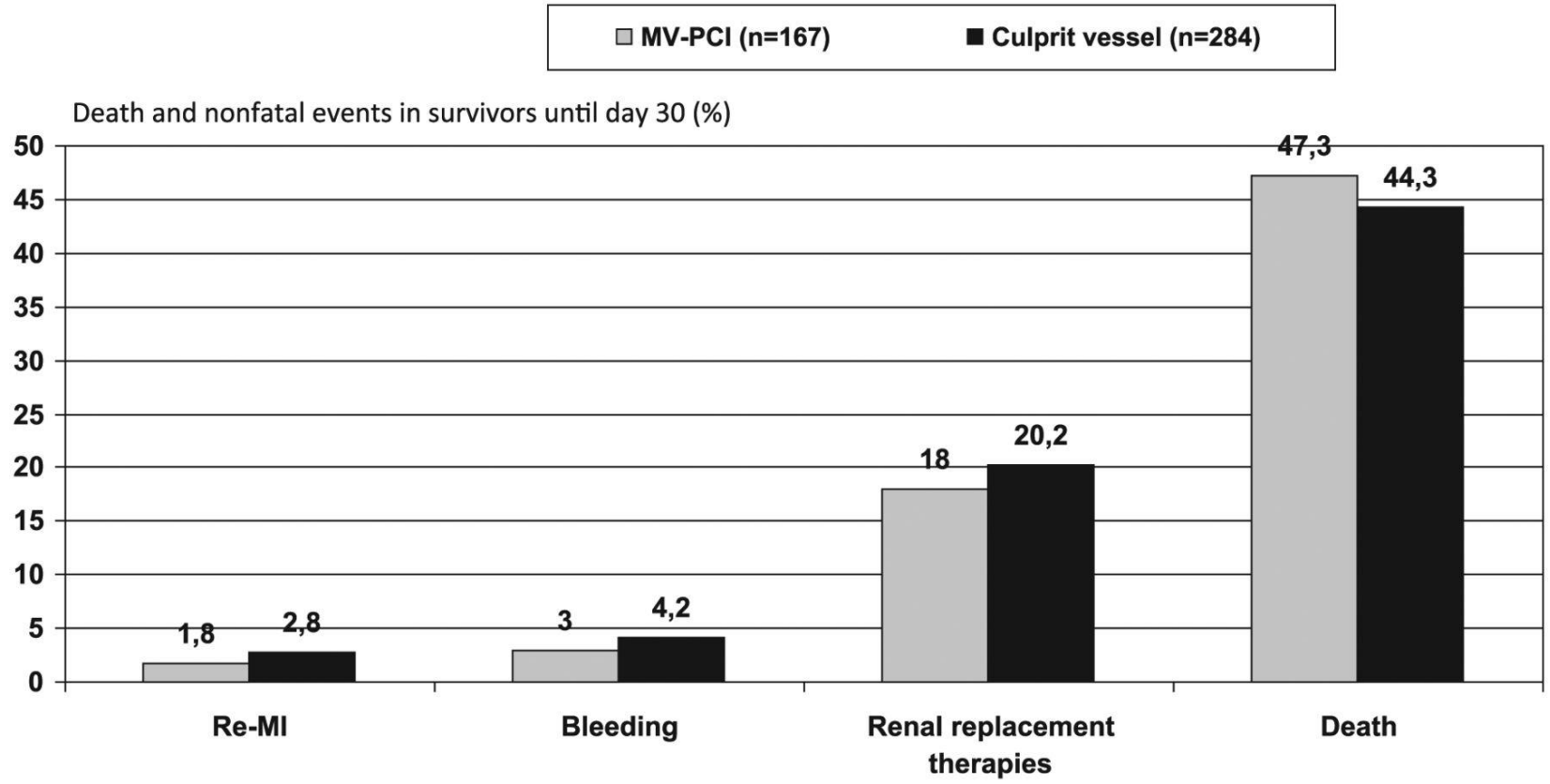
Mylotte et al. JACC CV Intv 2013;6:115-125

Multivessel PCI or Culprit Lesion Only PCI



Patients at risk							
MV-PCI	66	33	31	30	29	29	29
Culprit PCI	103	26	23	22	21	21	21

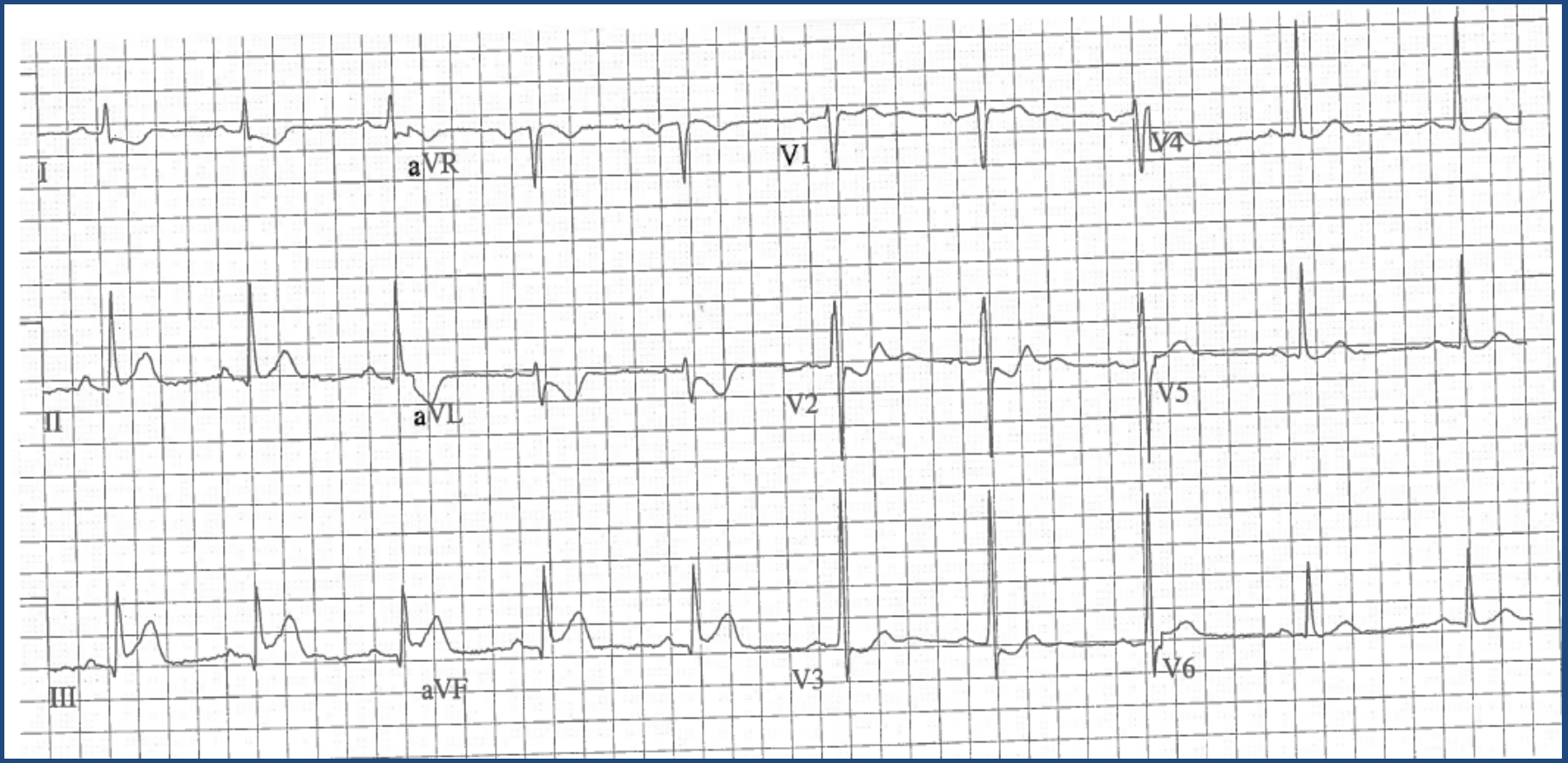
Figure 2. Clinical events until day 30 in patients treated with multivessel PCI or culprit lesion PCI. MV-PCI: Multivessel percutaneous coronary intervention; NF: non-fatal; MI: myocardial reinfarction.



Uwe Zeymer et al. European Heart Journal: Acute Cardiovascular Care 2016;2048872616668977

So what do we do with patients presenting with CGS and MVD ?

THE CASE



Unwell

Nausea vomiting

Sweating

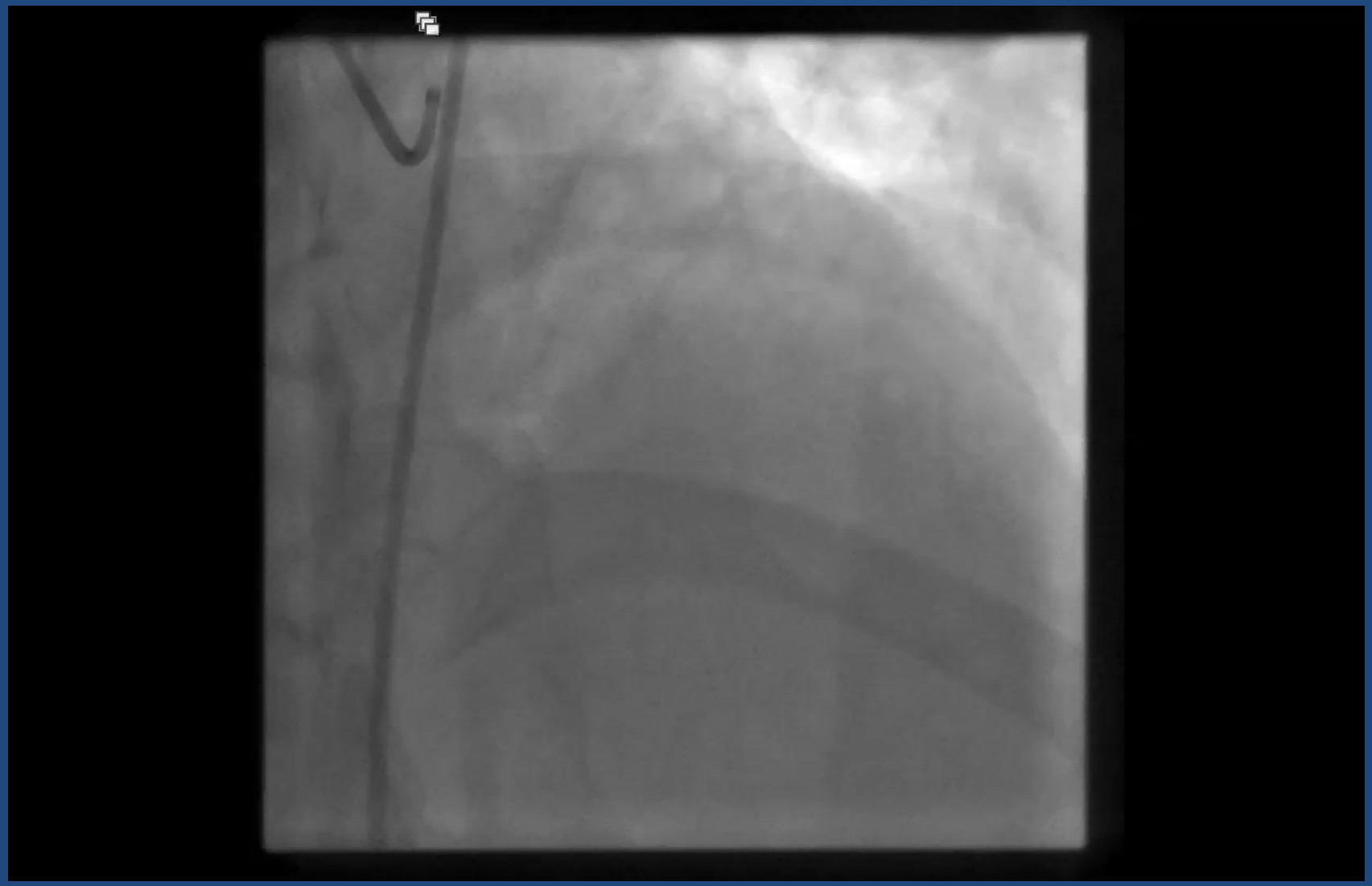
Cath lab

Femoral approach

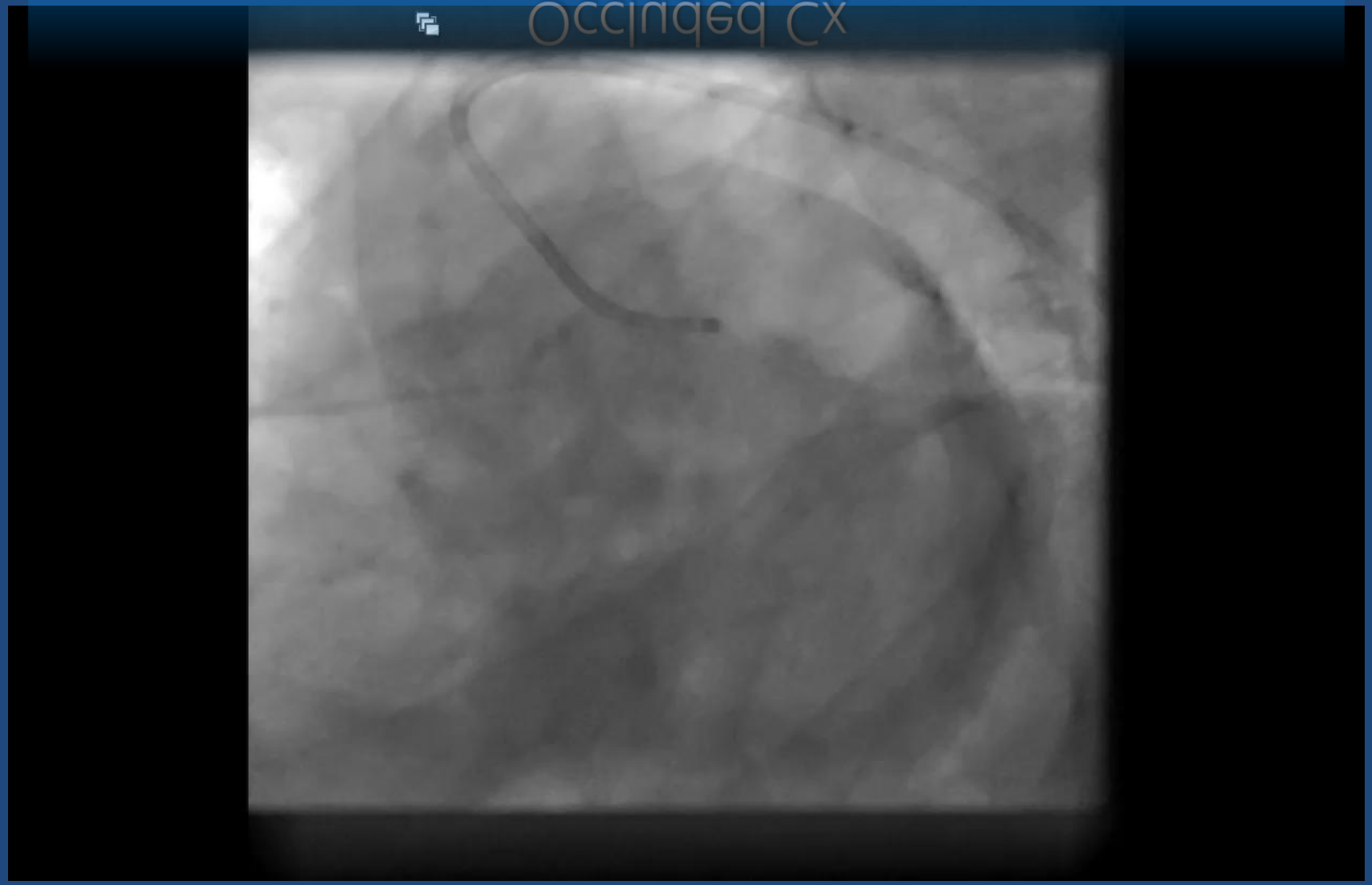
Ist Degree then 3:1 block

BP 95 mm Hg

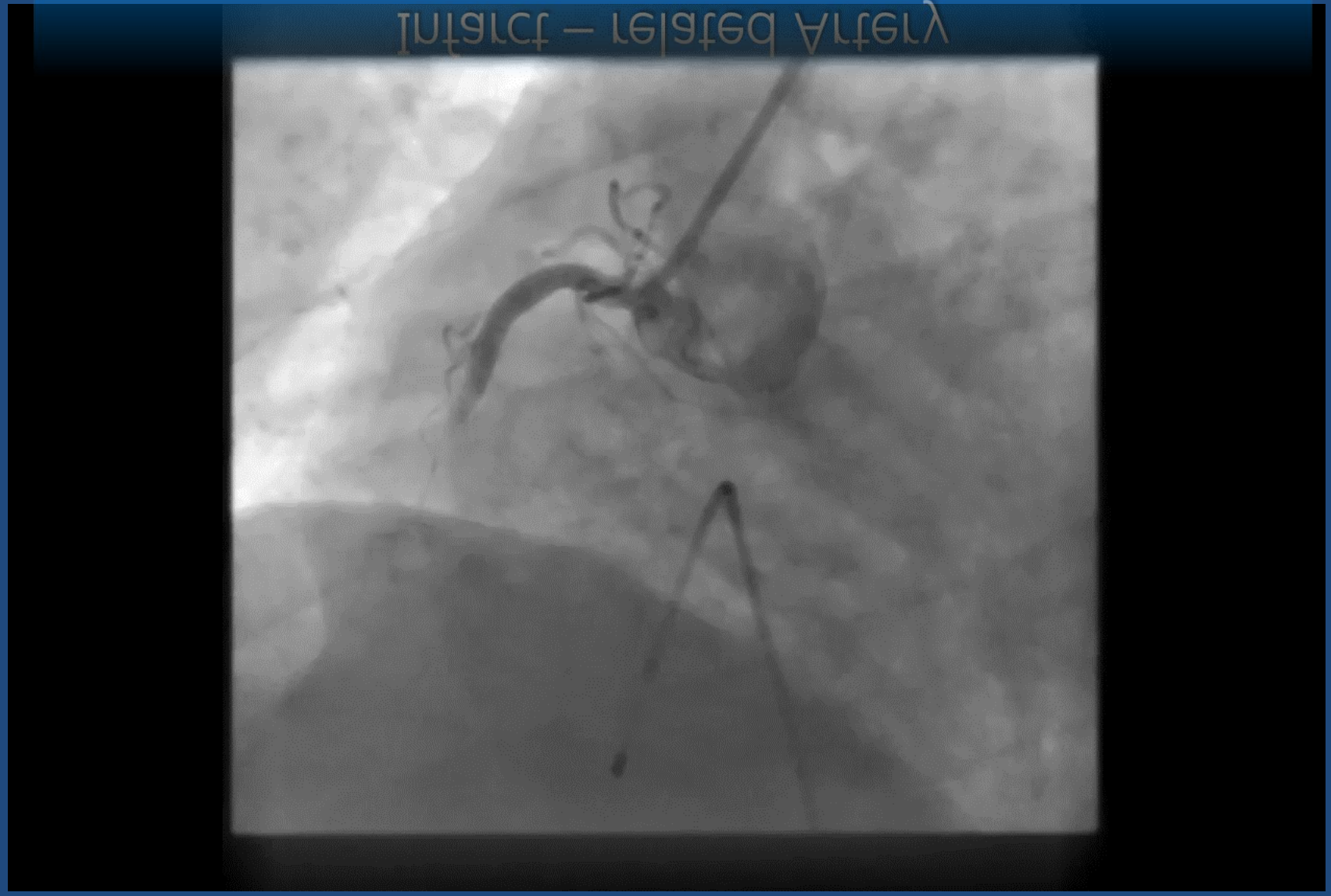
Non Infarct –related Artery



Occluded Cx



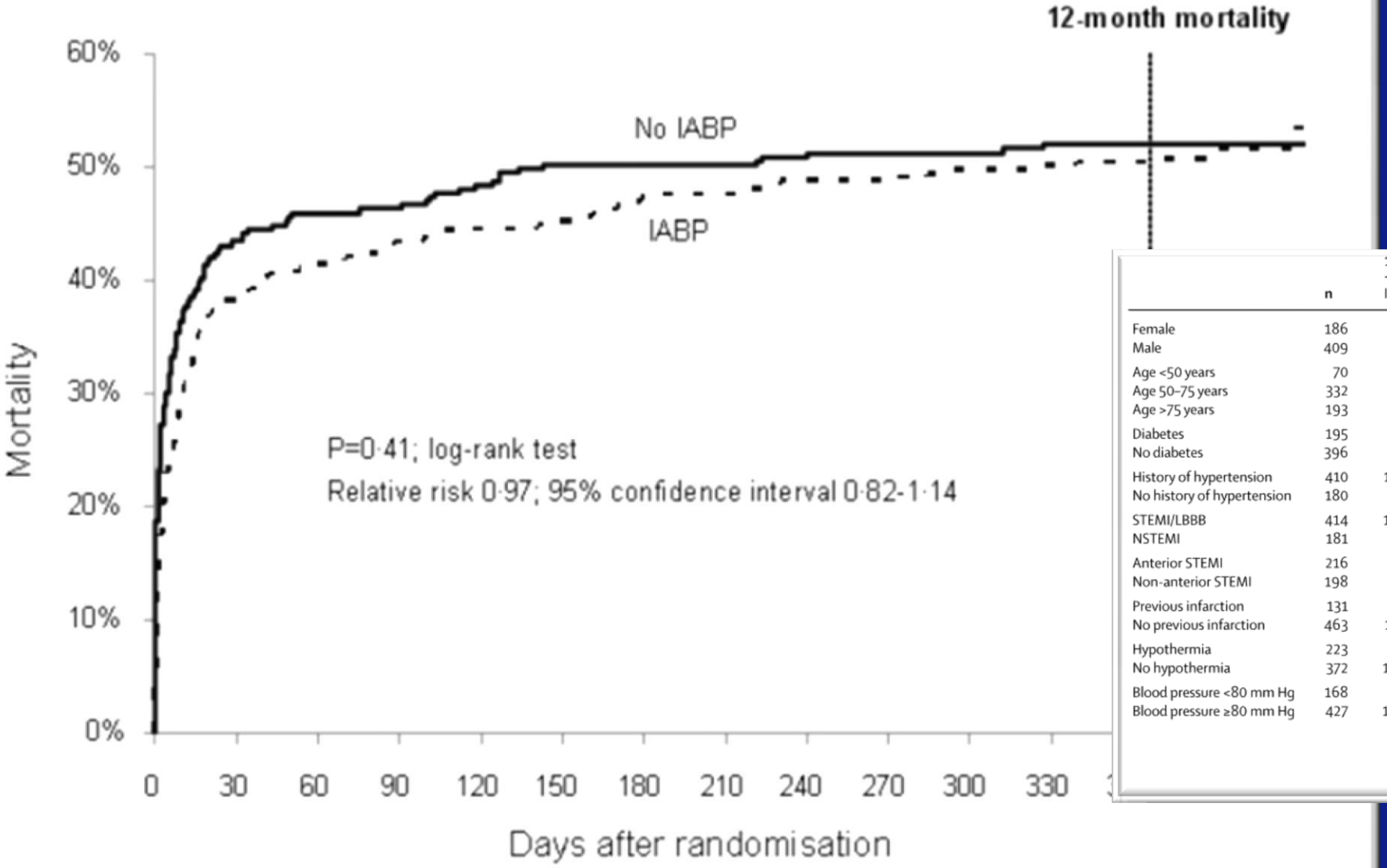
Infarct – related Artery



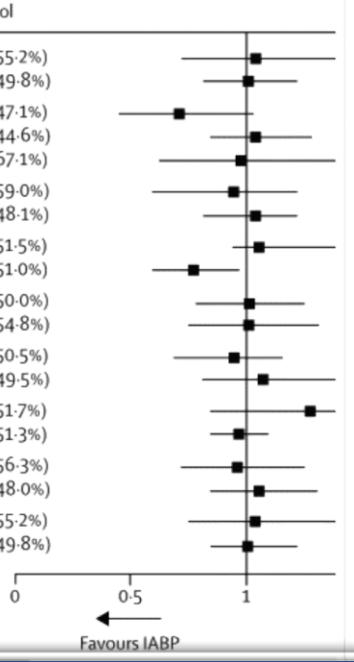
No IABP

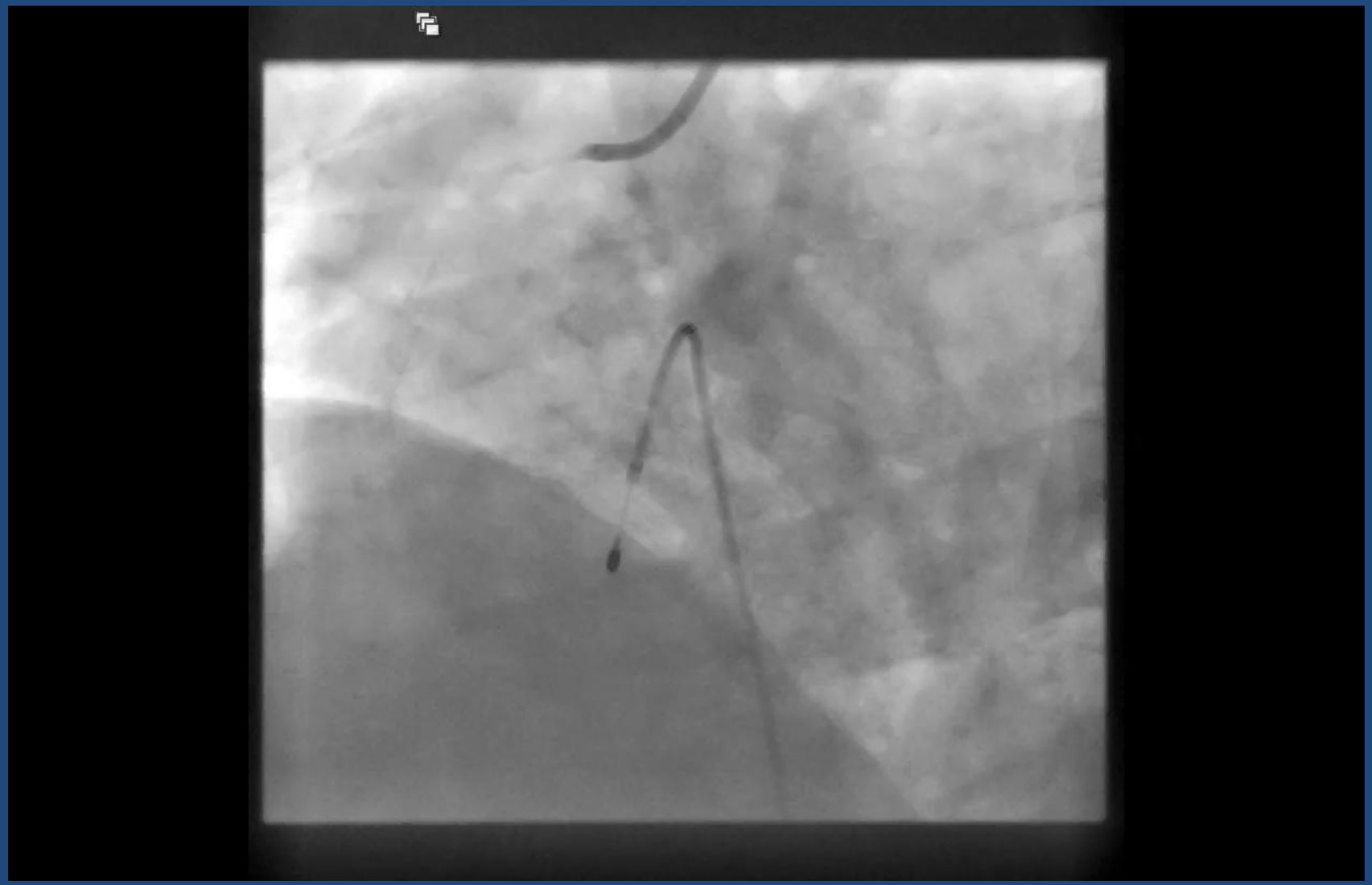
Recommendations	Class [a]	Level [b]	Ref [c]
In all patients with suspected cardiogenic shock, immediate ECG and echocardiography are recommended.	I	C	
All patients with cardiogenic shock should be rapidly transferred to a tertiary care center which has a 24/7 service of cardiac catheterization, and a dedicated ICU/CCU with availability of short-term mechanical circulatory support.	I	C	
In patients with cardiogenic shock complicating ACS an immediate coronary angiography is recommended (within 2 hours from hospital admission) with an intent to perform coronary revascularization.	I	C	
Continous ECG and blood pressure monitoring are recommended.		C	
Invasive monitoring with an arterial line is recommended.			
Fluid challenge (saline or Ringer's lactate, >200 ml/15–30 min) is recomme… overt fluid overload.			
Intravenous inotropic agents (dobutamine) may be considered to increase car…		C	
Vasopressors (norepinephrine preferable over dopamine) may be considered if there is … presence of persistent hypoperfusion.	IIb	B	558
IABP is not routinely recommended in cardiogenic shock.	III	B	585, 586
Short-term mechanical circulatory support may be considered in refractory cardiogenic shock depending on patient age, comorbidities and neurological function.	IIb	C	

Thiele H, Intra-aortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock (IABP-SHOCK II): final 12 month results of a randomised, open-label trial. Lancet 2013;382:1638–1645.

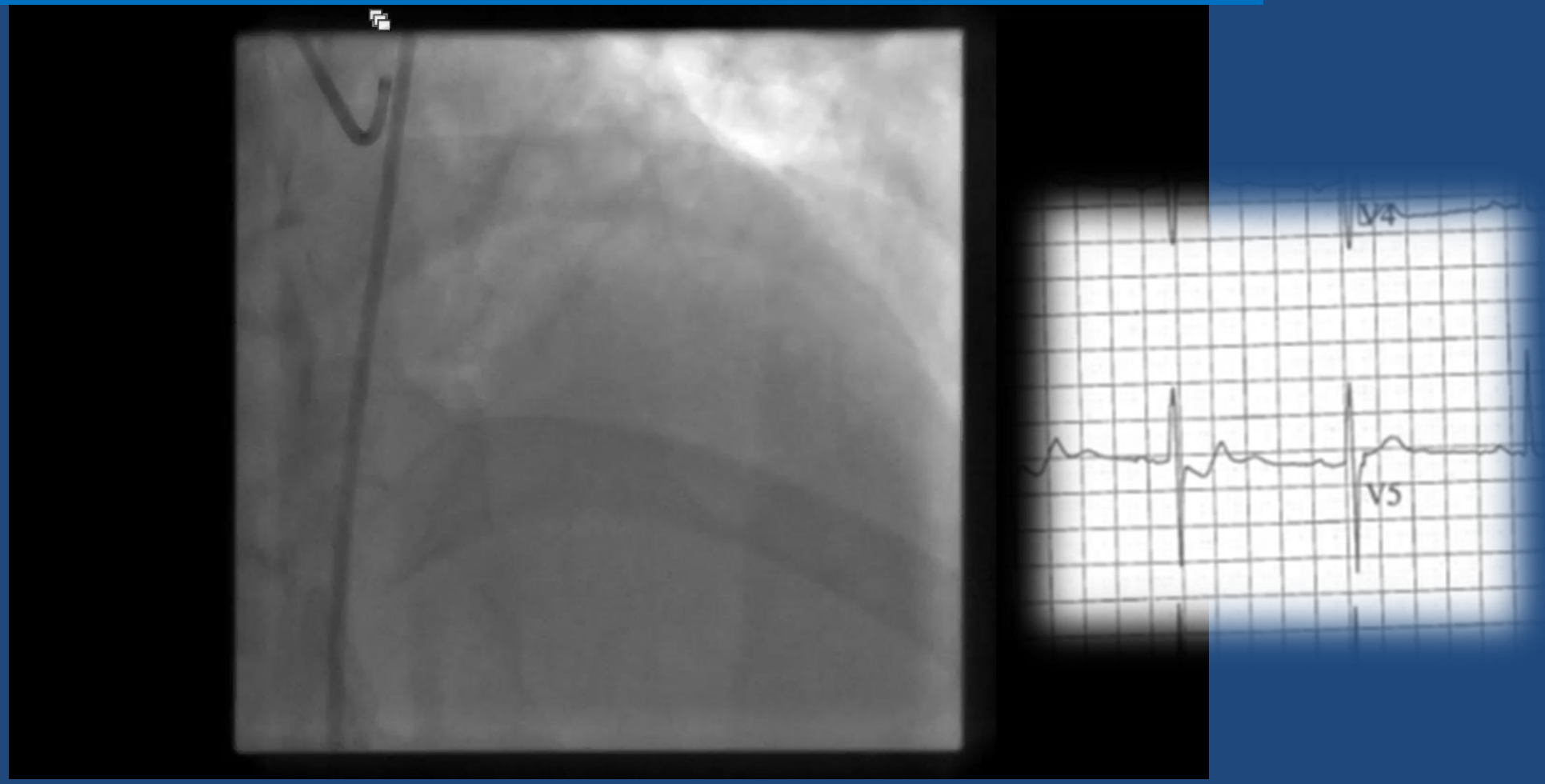


	n	12 month mortality, n (%) IABP	Control
Female	186	57 (57·6%)	48 (55·2%)
Male	409	98 (49·0%)	104 (49·8%)
Age <50 years	70	9 (25·0%)	16 (47·1%)
Age 50–75 years	332	75 (48·4%)	79 (44·6%)
Age >75 years	193	71 (65·7%)	57 (67·1%)
Diabetes	195	57 (54·3%)	53 (59·0%)
No diabetes	396	95 (50·0%)	99 (48·1%)
History of hypertension	410	122 (57·6%)	102 (51·5%)
No history of hypertension	180	29 (35·4%)	50 (51·0%)
STEMI/LBBB	414	102 (50·5%)	106 (50·0%)
NSTEMI	181	53 (54·6%)	46 (54·8%)
Anterior STEMI	216	53 (47·0%)	52 (50·5%)
Non-anterior STEMI	198	49 (55·1%)	54 (49·5%)
Previous infarction	131	44 (62·0%)	31 (51·7%)
No previous infarction	463	111 (49·0%)	121 (51·3%)
Hypothermia	223	55 (53·0%)	67 (56·3%)
No hypothermia	372	100 (51·3%)	85 (48·0%)
Blood pressure <80 mm Hg	168	47 (58·0%)	48 (55·2%)
Blood pressure ≥80 mm Hg	427	108 (49·5%)	104 (49·8%)

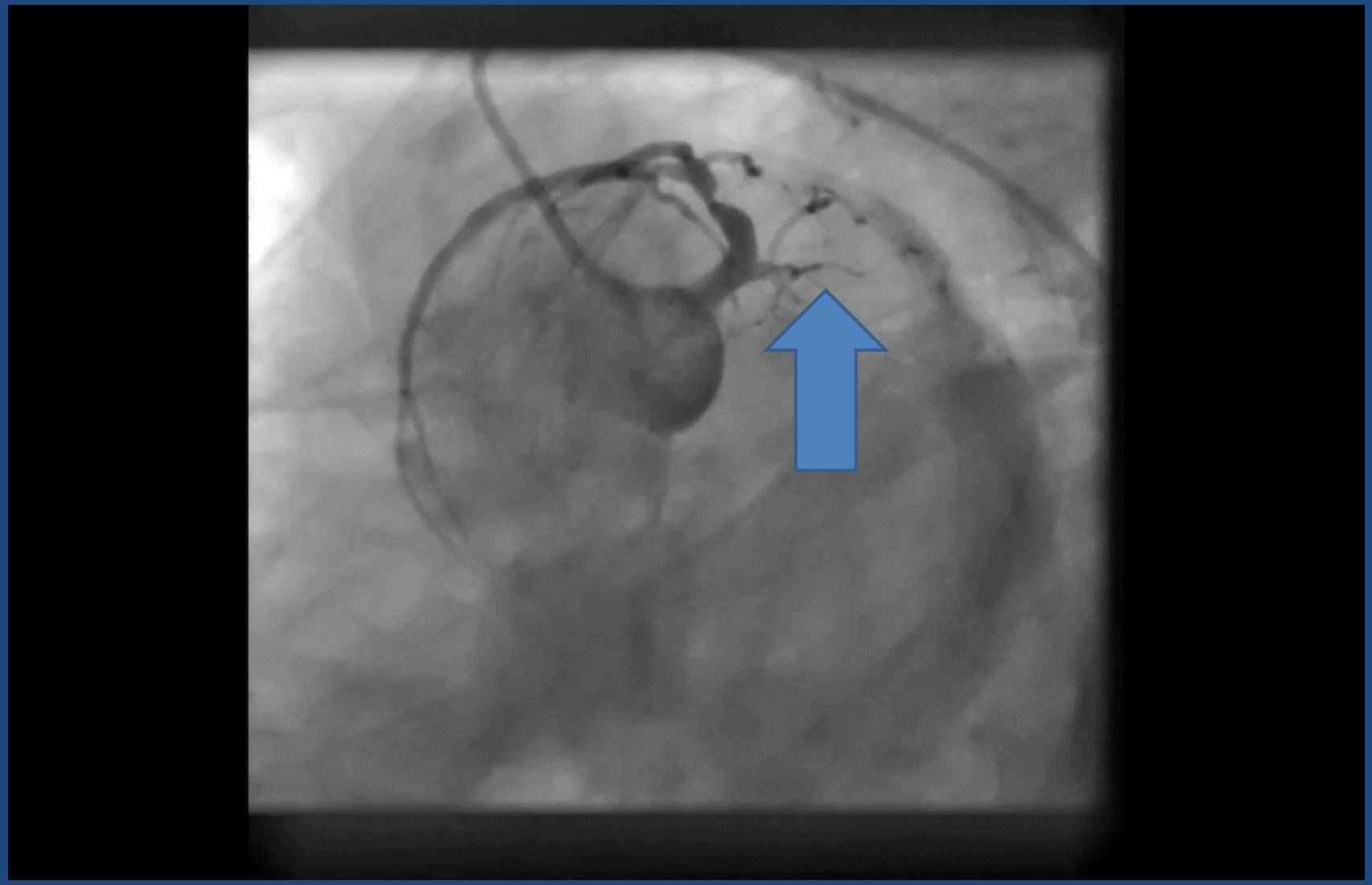




Non Infarct –related Artery



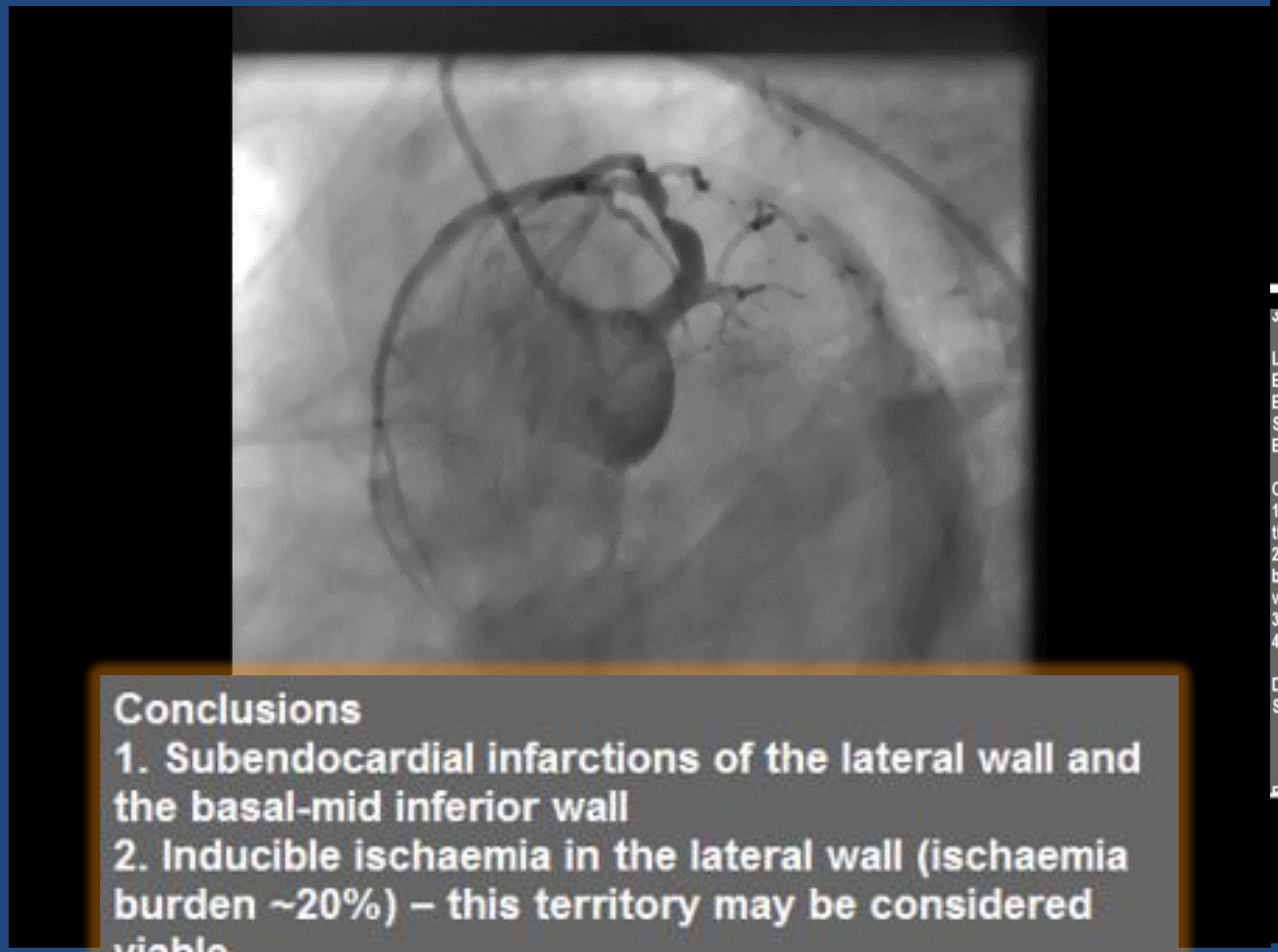
Would you do this ?
If so when ?
Now / as in patient / planned readmission ?



Would you do this Cx ?

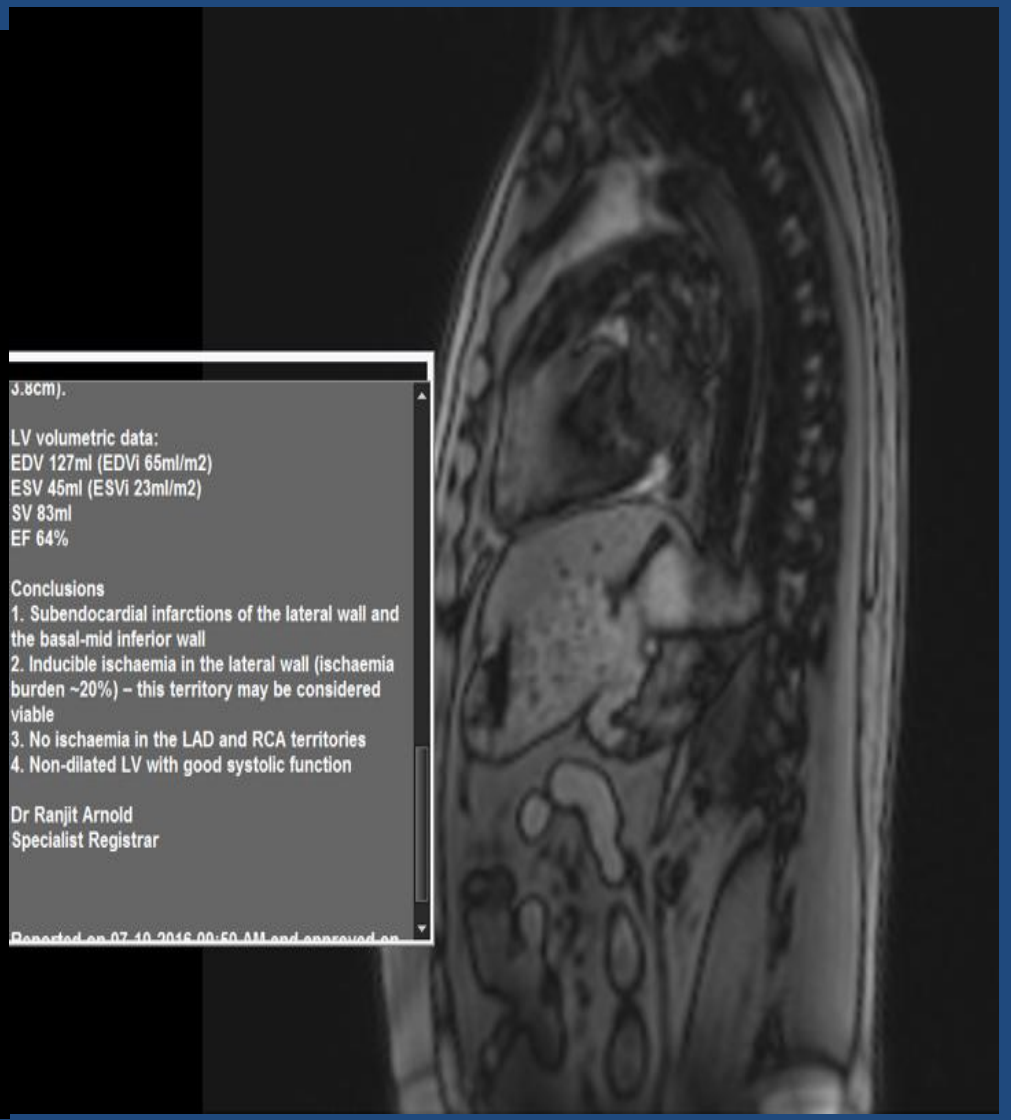
If so

When ? Now / in patient / planned readmission ?



Conclusions

1. Subendocardial infarctions of the lateral wall and the basal-mid inferior wall
2. Inducible ischaemia in the lateral wall (ischaemia burden ~20%) – this territory may be considered viable
3. No ischaemia in the LAD and RCA territories
4. Non-dilated LV with good systolic function



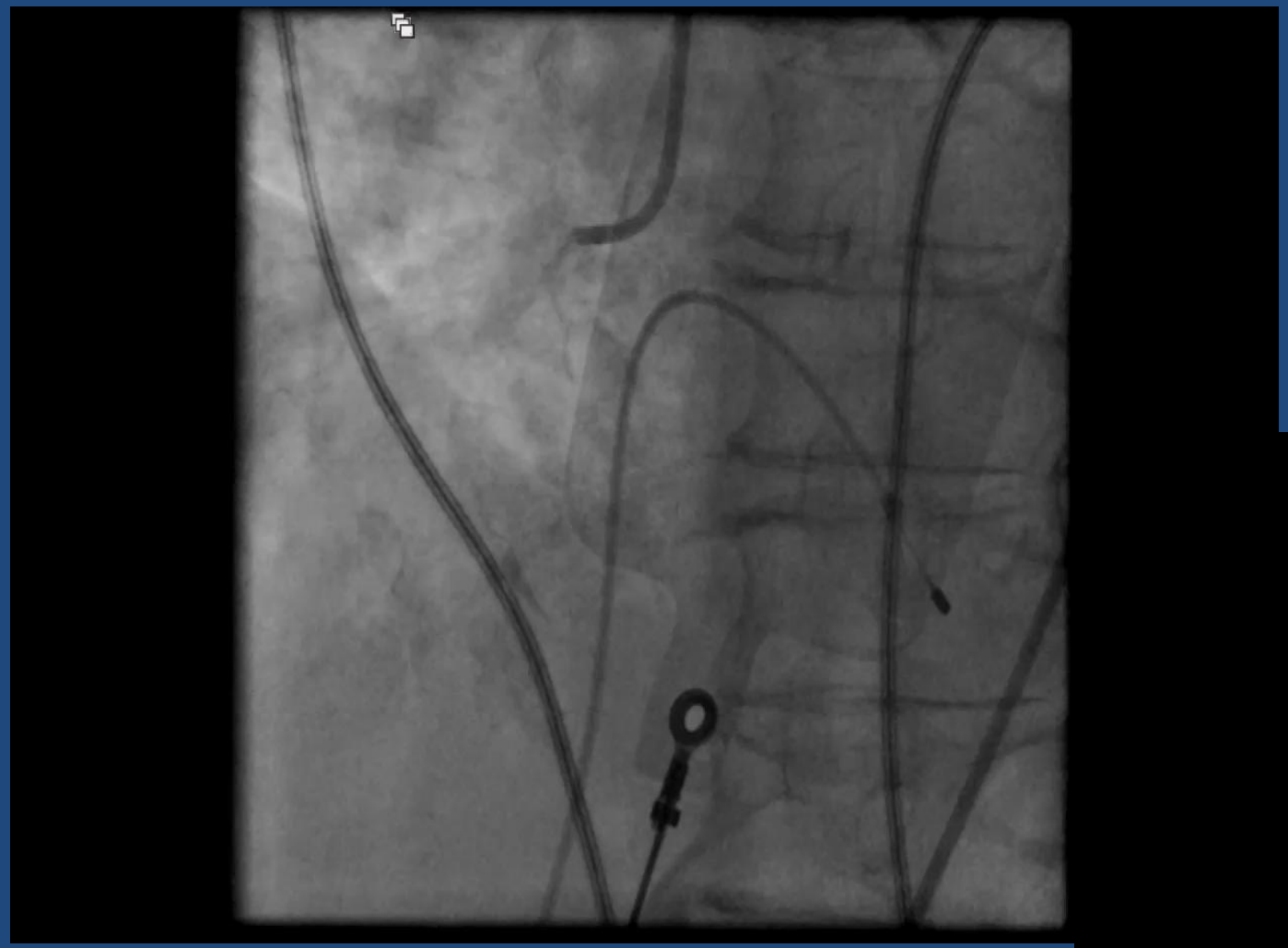
3.8cm).

LV volumetric data:
EDV 127ml (EDVi 65ml/m2)
ESV 45ml (ESVi 23ml/m2)
SV 83ml
EF 64%

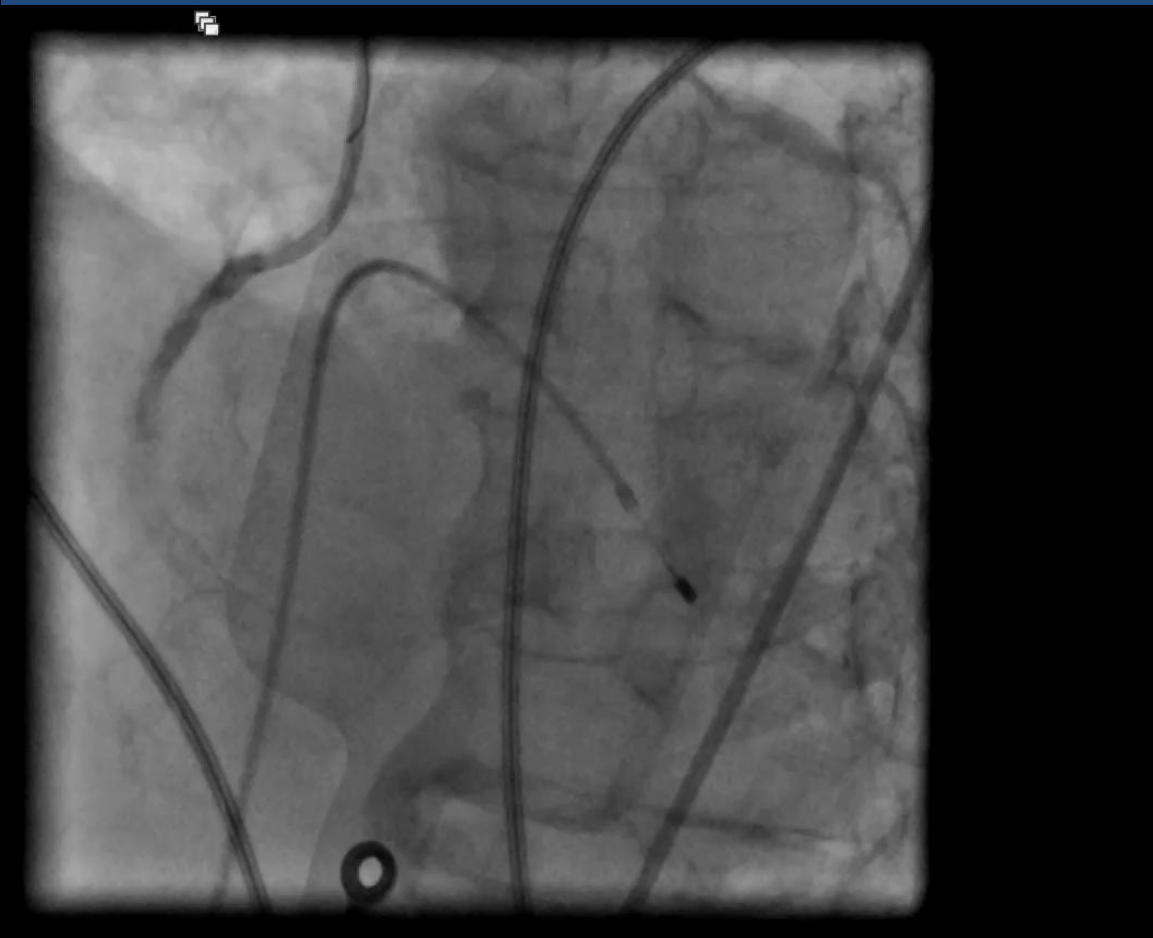
Conclusions
1. Subendocardial infarctions of the lateral wall and the basal-mid inferior wall
2. Inducible ischaemia in the lateral wall (ischaemia burden ~20%) – this territory may be considered viable
3. No ischaemia in the LAD and RCA territories
4. Non-dilated LV with good systolic function

Dr Ranjit Arnold
Specialist Registrar

Reported on 07-10-2016 09:50 AM and approved on



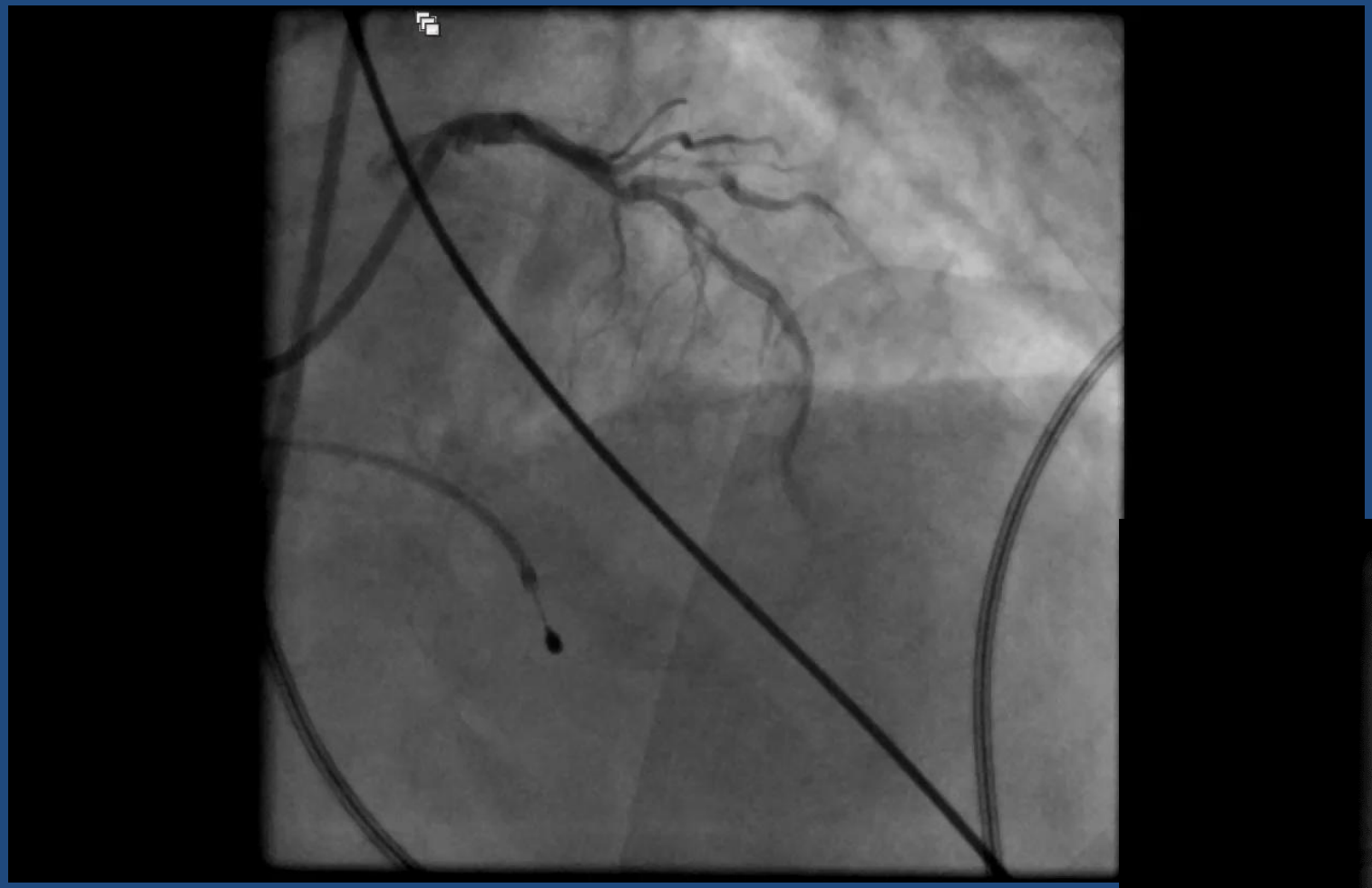
A slightly different case

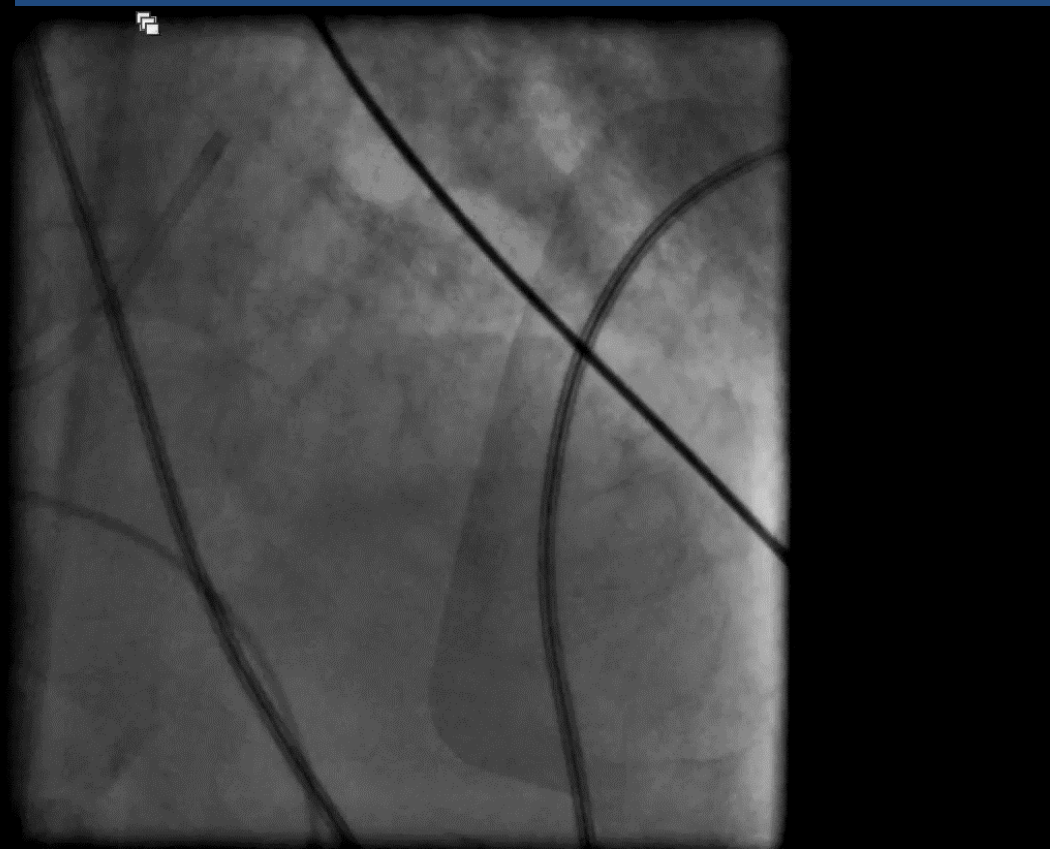


Male 84 years

Inferior STEMI CHB

BP 90 mmHg





Meta-Analysis of the Optimal Percutaneous Revascularization Strategy in Patients With Acute Myocardial Infarction, Cardiogenic Shock, and Multivessel Coronary Artery Disease

Giuseppe Tarantini, MD, PhD[a,*], Gianpiero D'Amico, MD[a], Paola Tellaroli, MSc, PhD[b], Claudia Colombo, MD[a], and Sorin J. Brener, MD[c]

Studies including patients with AMI and MV CAD complicated with CGS who received primary PCI were searched from 2000 to 2016

The primary end points were in-hospital/30- day and mid- to long-term (‡6 month) mortality

Fixed and random effects models were used for analysis. Ten studies (9 prospective and 1 retrospective) involving 6,068 patients

Zeymer, 2016 [15]
Zeymer, 2015 [16]
Park, 2015 [17]
Yang, 2013 [18]
Cavender, 2013 [19]
Mylotte, 2013 [20]
Bauer, 2012 [21]
van der Schaaf, 2010 [22]
Cavender, 2009 [23]
Webb, 2003 [24]

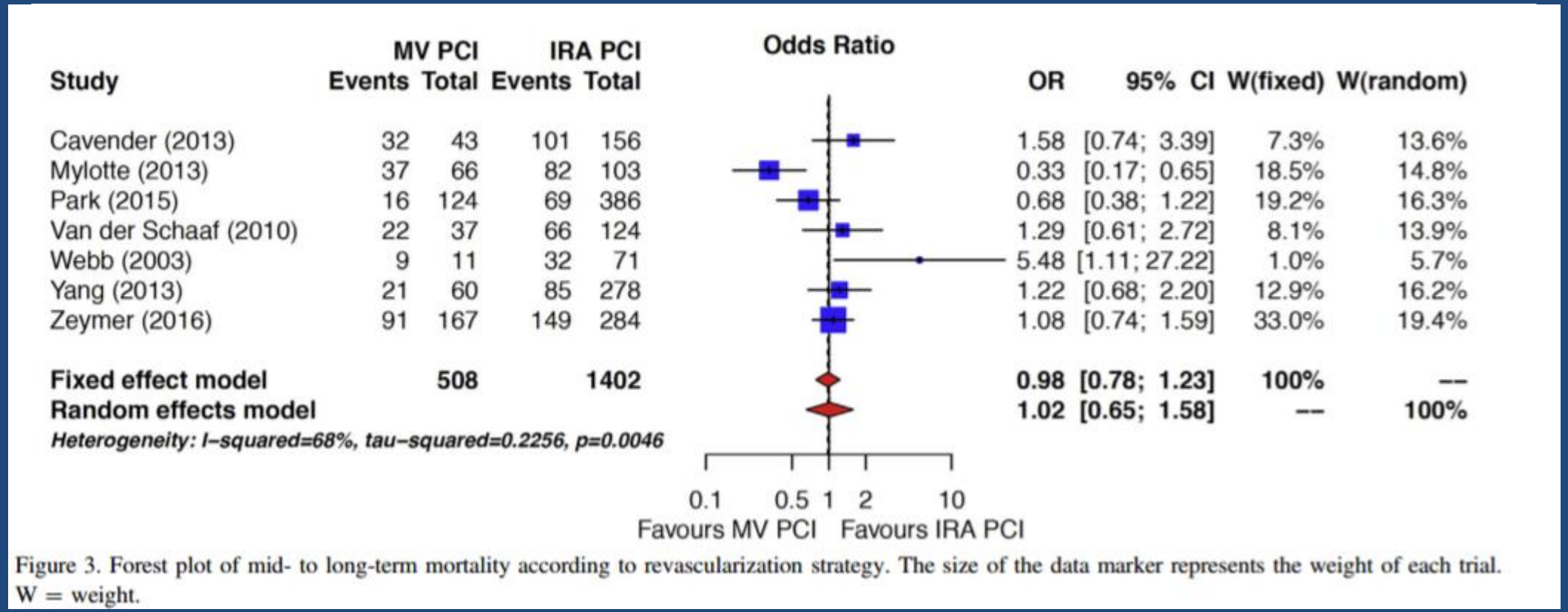


Figure 3. Forest plot of mid- to long-term mortality according to revascularization strategy. The size of the data marker represents the weight of each trial. W = weight.

In conclusion, in patients with AMI and MV CAD complicated by CS, the IRA-only PCI strategy seems to be associated with lower short-term, but not mid- to long-term mortality compared with MV PCI.

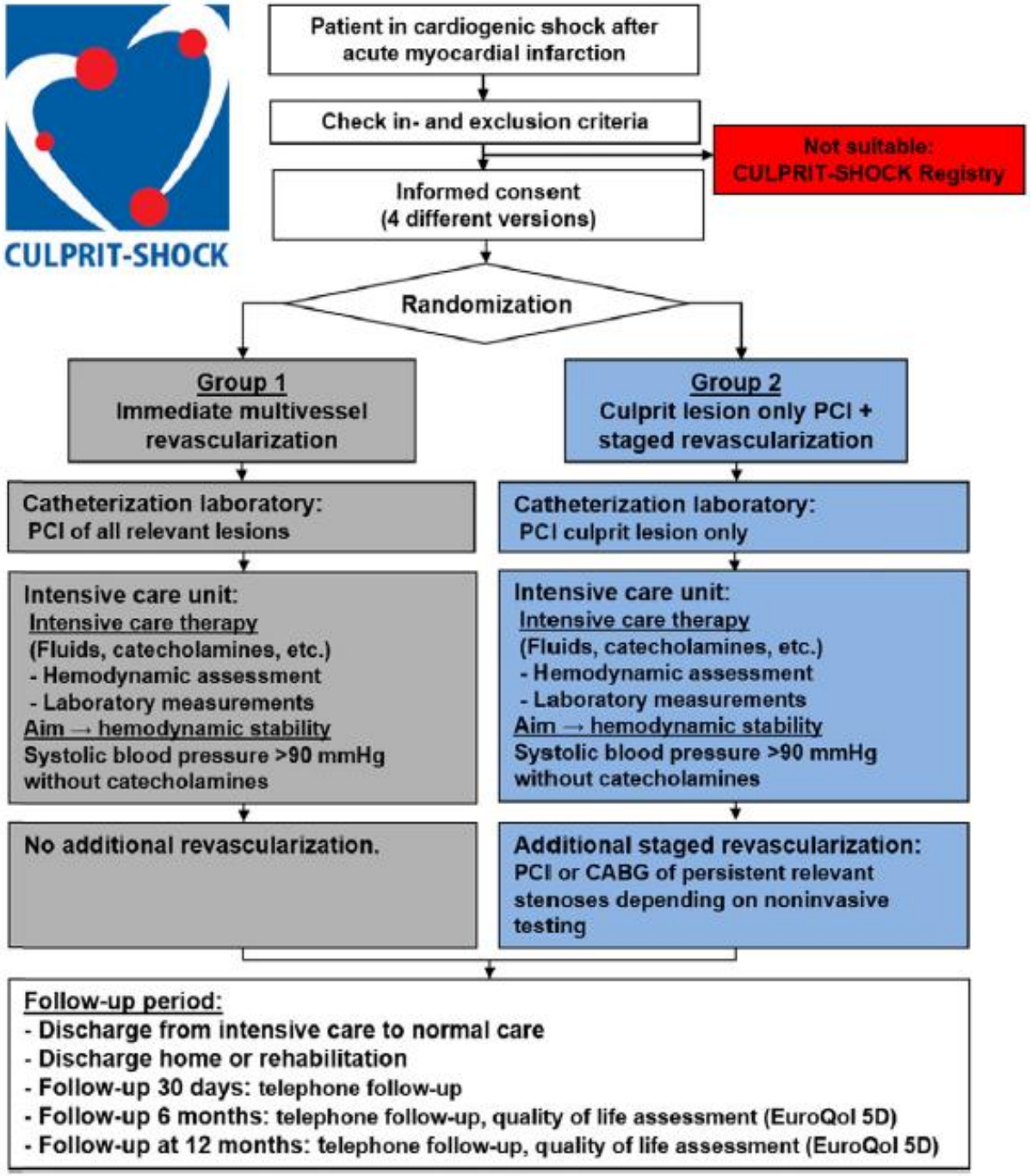
This finding is different from the revascularization strategy recommended by current professional guidelines and suggests the need for dedicated randomized clinical trials.

Multivessel versus culprit lesion only percutaneous revascularization plus potential staged revascularization in patients with acute myocardial infarction complicated by cardiogenic shock: Design and rationale of CULPRIT-SHOCK trial

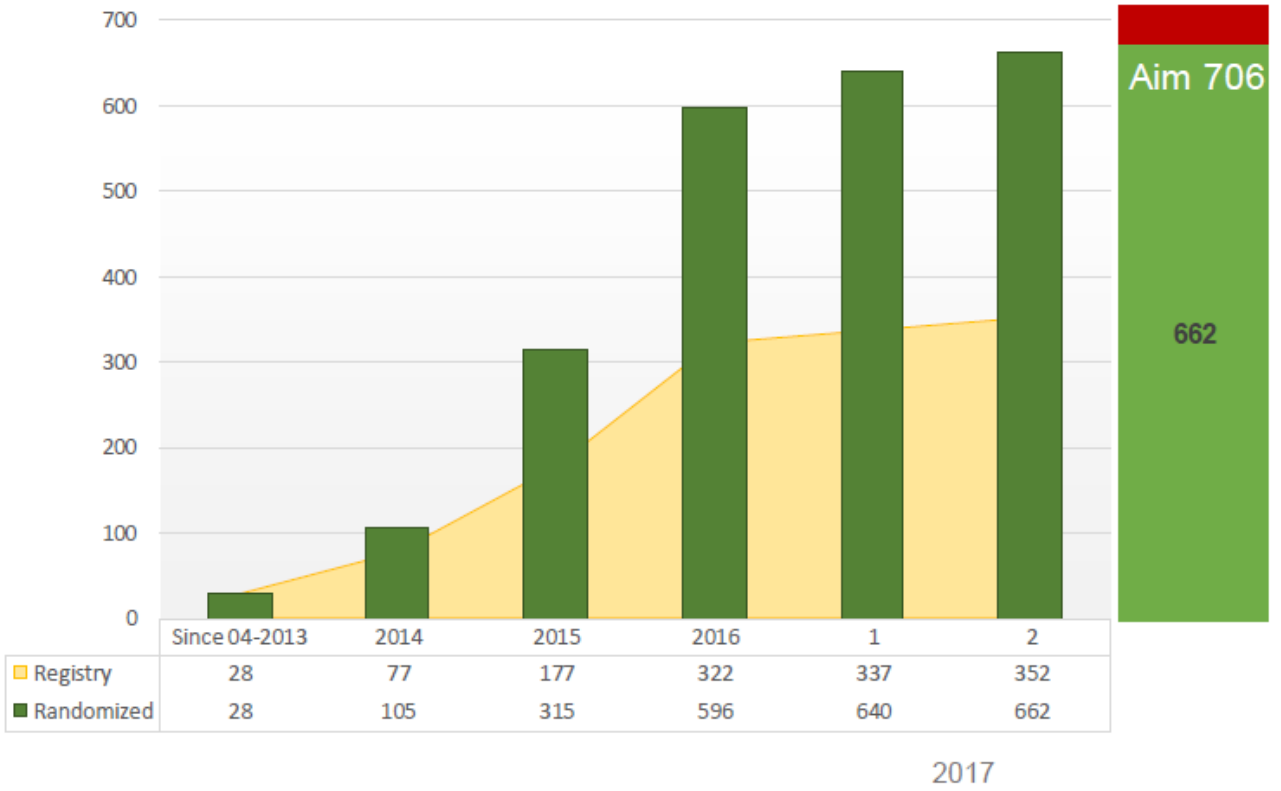
(Am Heart J 2016;172:160-9.)

Holger Thiele, MD,[a,b] Steffen Desch, MD,[a,b] Jan J. Piek, MD, PhD,[c] Janina Stepinska, MD,[d] Keith Oldroyd, MD,[e] Pranas Serpytis, MD,[f] Gilles Montalescot, MD,[g] Marko Noc, MD,[h] Kurt Huber, MD,[i] Georg Fuernau, MD,[a,b] Suzanne de Waha, MD,[a,b] Roza Meyer-Saraei, PhD,[a,b] Steffen Schneider, PhD,[j] Stephan Windecker, MD,[k] Stefano Savonitto, MD,[l] Andrew Briggs, PhD,[m] Patrizia Torremante[n] Christiaan Vrints, MD,[o] Gerhard Schuler, MD,[p] Uta Ceglarek, PhD,[q] Joachim Thiery, MD,[q] and Uwe Zeymer, MD[j,r], on behalf of the CULPRIT-SHOCK Investigators

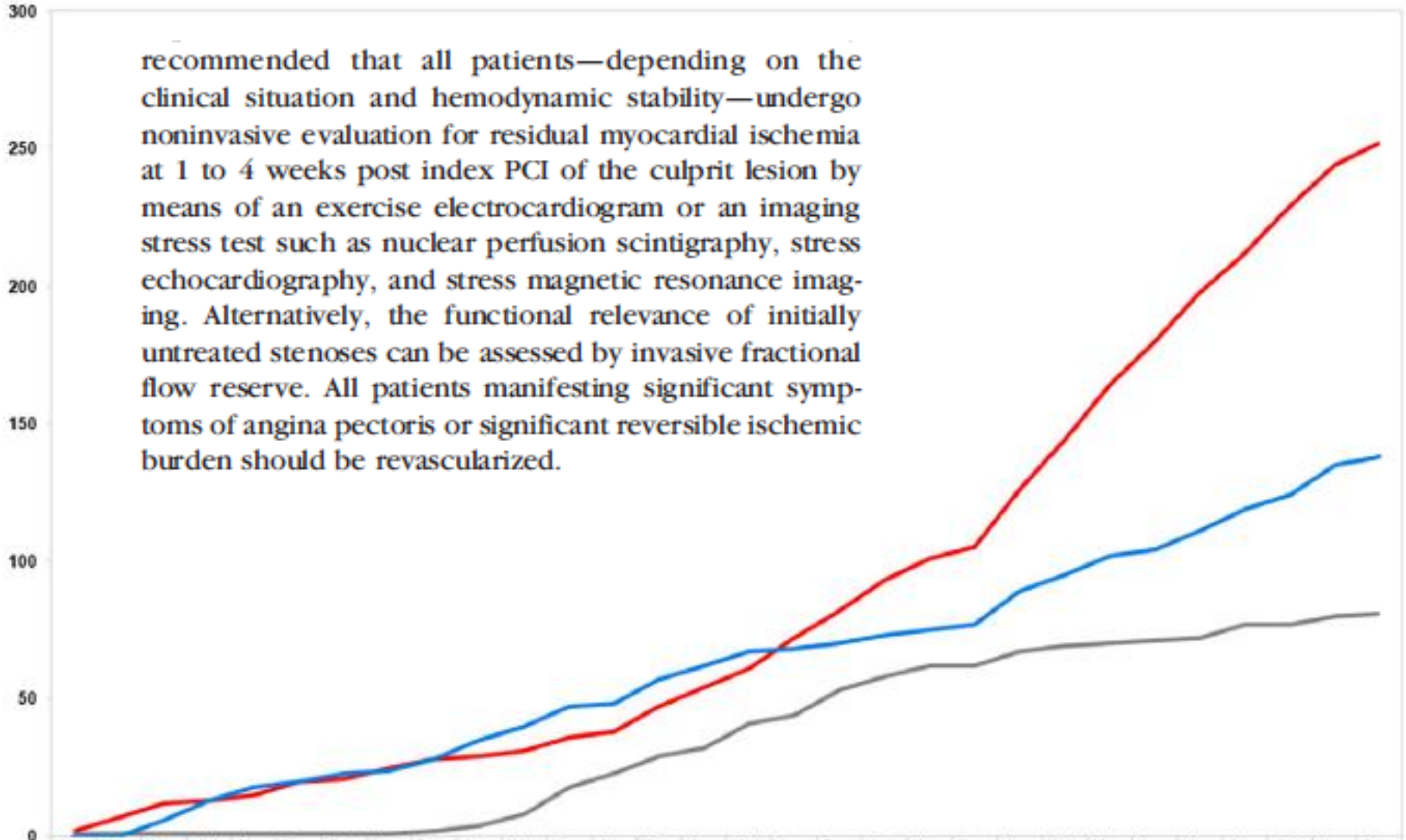
- MVD >70% in 2 major vessels (≥2mm)
- Identifiable culprit
  a. SBP < 90 mmHg > 30 mins or
  b. Catecholamine needed maintain BP > 90 mmHg
- Signs pulmonary congestion
- Signs impaired organ perfusion –
  altered mental state
  cold clammy
  oliguria
  serum lactate > 2.0 mmol/L



Total number of randomized patients	**662**
Aim of overall recruitment	**706**
% of recruitment aim (Current inclusion rate *100/706)	**93,7%**
Total number of registry patients	**352**



recommended that all patients—depending on the clinical situation and hemodynamic stability—undergo noninvasive evaluation for residual myocardial ischemia at 1 to 4 weeks post index PCI of the culprit lesion by means of an exercise electrocardiogram or an imaging stress test such as nuclear perfusion scintigraphy, stress echocardiography, and stress magnetic resonance imaging. Alternatively, the functional relevance of initially untreated stenoses can be assessed by invasive fractional flow reserve. All patients manifesting significant symptoms of angina pectoris or significant reversible ischemic burden should be revascularized.



	Apr-13	May-13	Jun-13	Jul-13	Aug-13	Sep-13	Oct-13	Nov-13	Dec-13	Jan-14	Feb-14	Mar-14	Apr-14	May-14	Jun-14	Jul-14	Aug-14	Sep-14	Oct-14	Nov-14	Dec-14	Jan-15	Feb-15	Mar-15	Apr-15	May-15	Jun-15	Jul-15	Aug-15	Sep-15
Centers	1	1	1	1	1	1	1	1	2	4	8	18	23	29	32	41	44	53	58	62	62	67	69	70	71	72	77	77	80	81
Randomized	2	7	12	13	15	20	21	25	28	29	31	36	38	47	54	61	72	82	93	101	105	126	144	164	180	198	212	229	244	252
Registry	0	0	6	13	18	20	23	24	28	35	40	47	48	57	62	67	68	70	73	75	77	89	95	102	104	111	119	124	135	138

Revascularisation & CGS

- P-PCI mandated
- MVD common
- Comes in multiple guises
- Intuitive to treat
- Data are variable

- Trial needed
  COMPLETED !!!
- May not address all the issues or all cases as heterogeneous mix

- What do I do ?

Doable versus un-wellness