Coronary Angiography after Cardiac Arrest without ST-Segment Elevation: the COACT trial

On behalf of the **COACT investigators**

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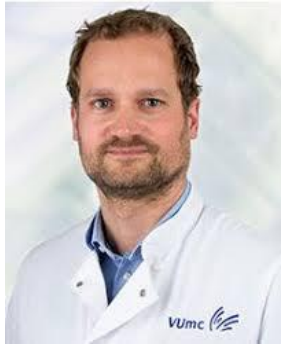
Disclosure statement of financial interest

I, Jorrit Lemkes, 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.



The COACT trial was supported by unrestricted research grants from the Netherlands Heart Institute, Biotronik, and AstraZeneca.

Background

- OHCA is a leading cause of death in Europe and the United States.
- Despite advances in the field of resuscitation and intensive care management, the outcome in patients after OHCA remains poor.
- Among patients with ROSC a mortality of 40% has been reported.[1]
- The most frequent cause of cardiac arrest is ischemic heart disease, and coronary artery disease has been reported in up to 70% of patients after OHCA.[2]

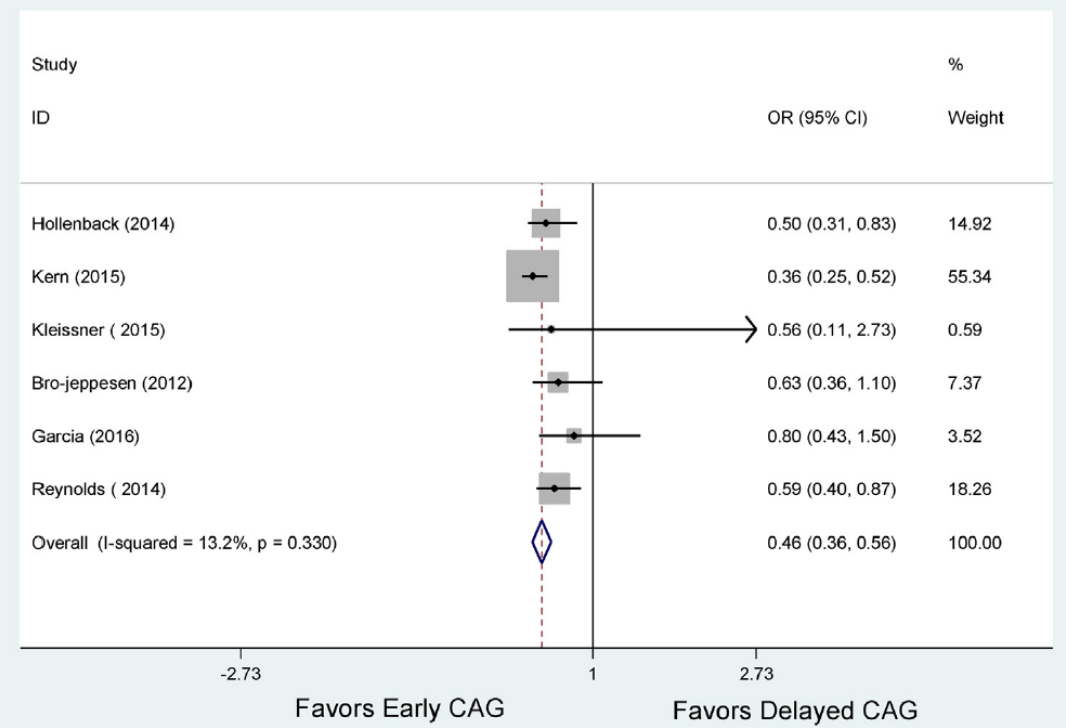
1. Patel N, *et al. JAMA Cardiol,* 2016; **2.** Spaulding CM, *et al. N Engl J Med,* 1997.

Background

- Guidelines recommend immediate coronary angiography with PCI in patients who present with STEMI and cardiac arrest (class 1 LOE B).[1,2]
- In patients with cardiac arrest without ST-elevation, guidelines also recommend emergency angiography (weak recommendation, very-low-quality evidence).[3]
- This is based on observational data and no randomized trials have been performed.

1. Ibanez B, *et al. EHJ,* 2018; **2.** O'Gara PT, *et al. J Am Coll Cardiol,* 2013; **3.** Welsford M*, et al. Circulation*, 2015

Observational studies favor early CAG

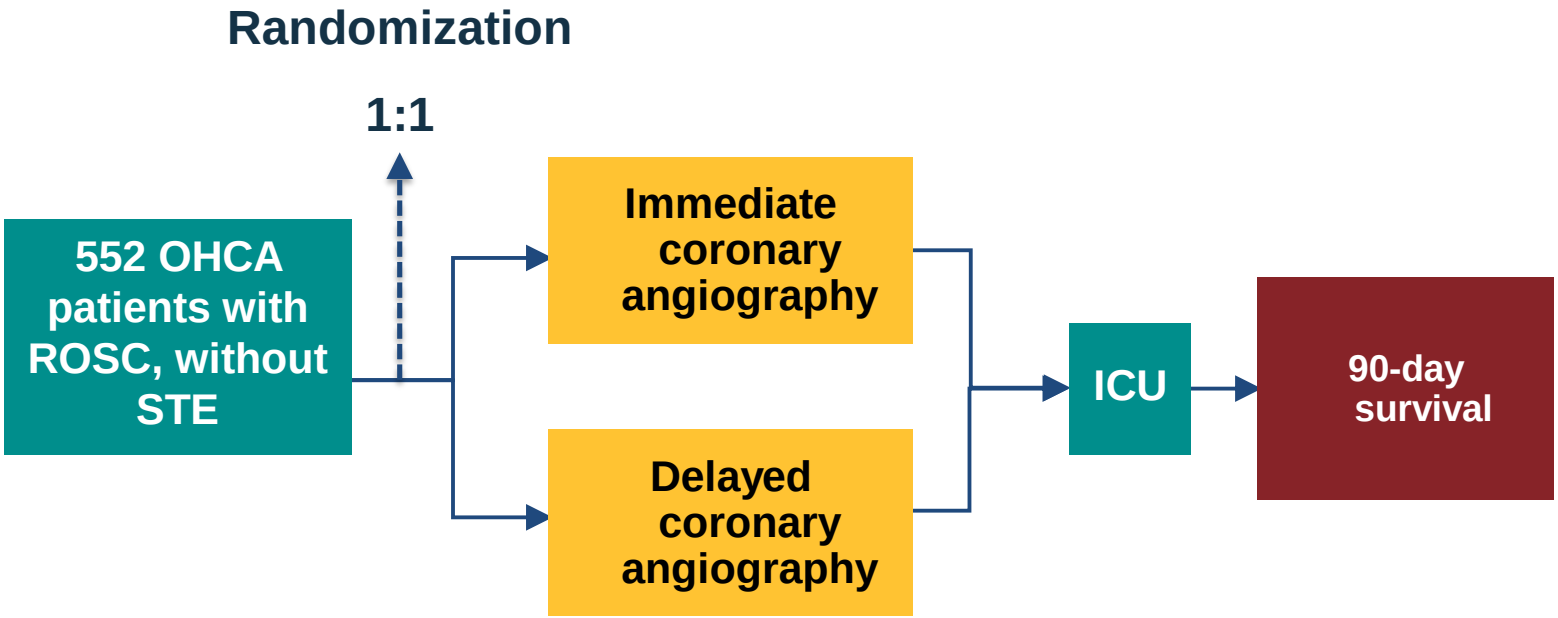


Khan M, *et al. Resuscitation,* 2017

Study hypothesis

- We therefore hypothesize that immediate coronary angiography will improve survival.
- We calculated that 251 patients would need to be enrolled in each group to give the trial 85% power to detect a 40% difference between the immediate and delayed angiography group in terms of survival.
- The sample size was increased by 10% to a total of 552 patients to account for loss of patients to follow-up.

Trial design



Trial organization

Steering committee

Niels van Royen (chair), Jorrit Lemkes, Heleen Oudemans-van Straaten, Lucia Jewbali, Michiel Voskuil, Martijn Meuwissen.

Data safety monitoring board

Freek Verheugt (chair), Eric Boersma (statistician), Ruud Koster.

Trial statistician

Peter van de Ven.

Study coordinators

Gladys Janssens, Nina van der Hoeven.

Key in- and exclusion criteria

Inclusion criteria

- Age >18 years.
- Comatose patients (Glasgow coma score <8) with ROSC after OHCA.
- Ventricular tachycardia or ventricular fibrillation as initial arrest rhythm. Including patients treated with an AED.

Exclusion criteria

- Signs of STEMI on the ECG at the emergency department.
- Hemodynamic instability unresponsive to medical therapy.
- Refractory ventricular arrhythmia.
- An obvious or suspected non-coronary cause of the arrest.
- Suspected or confirmed acute intracranial bleeding or acute stroke.

End points

Primary endpoint:

- Survival at 90 days

Secondary endpoints:

- Survival at 90 days with good cerebral performance or moderate disability
- TIMI major bleeding
- Recurrence of ventricular tachycardia
- Occurrence of acute kidney injury and need for renal-replacement therapy
- Time to target temperature
- Duration of inotropic/catecholamine support
- Duration of mechanical ventilation
- Myocardial injury
- Markers of shock

Trial flow diagram

552 patients with OHCA and ROSC without signs of ST-elevation were randomized (1:1)

Allocation

Immediate coronary angiography (n=280)
- 267 patients with immediate CAG (95.4%)
- 13 patients with delayed CAG (4.6%)
  - Logistical reason (n=3)
  - Physician decision (n=6)
  - Protocol violation (n=4)

Informed consent

Informed consent (n=273)
- 273 patients with full informed consent
- 7 patients/families refused informed consent

3-month follow-up

Additional patients lost to follow-up (n=0)

Primary end point analysis

Analyzed (n=273, 97.5%)
- 0 patients excluded from intention to treat analysis.

Allocation

Delayed coronary angiography (n=272)
- 269 patients with delayed CAG (98.9%)
  - Urgent CAG due to symptoms (n=38)
- 3 patients with immediate CAG (1.1%)
  - Logistical reason (n=1)
  - Physician decision (n=1)
  - Protocol violation (n=1)

Informed consent

Informed consent (n=265)
- 265 patients with full informed consent
- 7 patients/families refused informed consent

3-month follow-up

Additional patients lost to follow-up (n=0)

Primary end point analysis

Analyzed (n=265, 97.4%)
- 0 patients excluded from intention to treat analysis.

Baseline characteristics

	Immediate Angiography Group (N=273)	Delayed Angiography Group (N=265)
Age – years	65.7±12.7	64.9±12.5
Male sex – no. (%)	223 (81.7%)	202 (76.2%)
Hypertension – no./total no. (%)	131/269 (48.7%)	126/265 (47.5%)
Previous myocardial infarction – no. (%)	73 (26.7%)	76 (28.7%)
Previous CABG – no./total no. (%)	43/272 (15.8%)	24/265 (9.1%)
Previous PCI – no./total no. (%)	46/272 (16.9%)	60/264 (22.7%)
Previous CAD – no. (%)	99 (36.3%)	96 (36.2%)
Previous CVA – no./total no. (%)	19/272 (7.0%)	15/265 (5.7%)
Diabetes Mellitus – no./total no. (%)	55/272 (20.2%)	44/265 (16.6%)
Smoker – no./total no. (%)	50/249 (20.1%)	67/249 (26.9%)
Hypercholesterolemia – no./total no. (%)	70/270 (25.9%)	78/263 (29.7%)
Peripheral artery disease – no./total no. (%)	16/272 (5.9%)	23/265 (8.7%)
Arrest witnessed – no. (%)	218 (79.9%)	203 (76.6%)
Median time from arrest to BLS (IQR) – min	2 (1-5)	2 (1-5)
Median time from arrest to ROSC (IQR) – min	15 (9-21)	15 (8-20)

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Procedures, treatments and characteristics of coronary artery disease

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Median time from arrest to CAG (IQR) – hr	2.3 (1.8-3.0)	121.9 (52.0-197.3)
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Arteries with stenosis – no./total no. (%)		
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Acute thrombotic occlusion – no./total no. (%)	9/265 (3.4%)	13/172 (7.6%)‡
Chronic total occlusion – no./total no. (%)	100/265 (37.7%)	58/172 (33.7%)
Revascularization treatment – no. (%)		
PCI	90 (33.0%)	64 (24.2%)
CABG	17 (6.2%)	23 (8.7%)
Medical or conservative treatment	168 (61.5%)	179 (67.5%)

† 38 of these patients received urgent intervention because of cardiac deterioration, * 95% of patients who survived until hospital discharge.
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Medical treatment during hospitalization

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Salicylates – no. (%)	207 (75.8%)	230 (86.8%)
P2Y12 inhibitor – no. (%)	159 (58.2%)	188 (70.9%)
Unfractionated heparin/LMWH – no. (%)	246 (90.1%)	234 (88.3%)
Bivalirudin – no. (%)	2 (0.7%)	2 (0.8%)
Glycoprotein IIb/IIIa inhibitor – no. (%)	17 (6.2%)	7 (2.6%)
Statins – no. (%)	173 (63.4%)	182 (68.7%)
Betablocker – no./total no. (%)	187/272 (68.8%)	186/264 (70.5%)
ACE-inhibitor/angiotensin II receptor blocker – no./total no. (%)	164/272 (60.3%)	169/264 (64.0%)
Amiodarone – no./total no. (%)	74/272 (27.2%)	83/265 (31.3%)

Medical treatment during hospitalization

	Immediate Angiography Group (N=273)	Delayed Angiography Group (N=265)
Salicylates – no. (%)	**207 (75.8%)**	**230 (86.8%)**
P2Y12 inhibitor – no. (%)	**159 (58.2%)**	**188 (70.9%)**
Unfractionated heparin/LMWH – no. (%)	246 (90.1%)	234 (88.3%)
Bivalirudin – no. (%)	2 (0.7%)	2 (0.8%)
Glycoprotein IIb/IIIa inhibitor – no. (%)	17 (6.2%)	7 (2.6%)
Statins – no. (%)	173 (63.4%)	182 (68.7%)
Betablocker – no./total no. (%)	187/272 (68.8%)	186/264 (70.5%)
ACE-inhibitor/angiotensin II receptor blocker – no./total no. (%)	164/272 (60.3%)	169/264 (64.0%)
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Primary end point

	Immediate Angiography Group (N=273)	Delayed Angiography Group (N=265)	Effect Size (95% CI)	P value
Survival at 90 days – no. (%)	176 (64.5%)	178 (67.2%)	OR, 0.89 (0.62-1.27)	0.51

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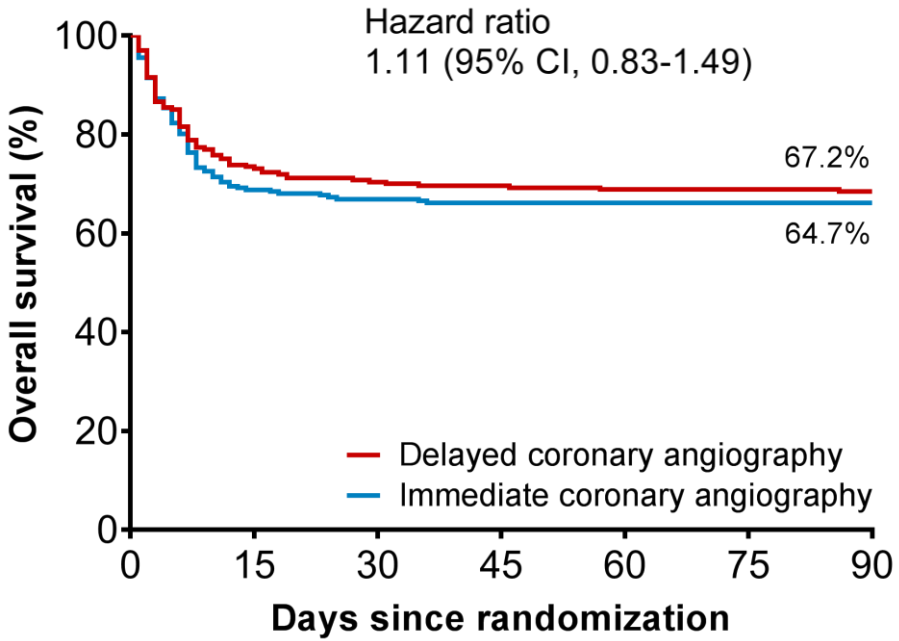
Overall survival



No. at risk							
Immediate	273	183	178	176	176	176	176
Delayed	265	191	183	181	179	179	178

Secondary end points

	Immediate Angiography Group (N=273)	Delayed Angiography Group (N=265)	Effect Size (95% CI)*
Survival with good cerebral performance or moderate disability – no./total no. (%)	171/272 (62.9%)	170/264 (64.4%)	OR, 0.94 (0.66-1.31)
TIMI-major bleeding – no. (%)	7 (2.6%)	13 (4.9%)	OR, 0.51 (0.20-1.30)
Recurrence of VT resulting in defibrillation or electrical cardioversion – no. (%)	21 (7.7%)	16 (6.0%)	OR, 1.30 (0.66-2.54)
Need for renal replacement therapy – no. (%)	8 (2.9%)	11 (4.2%)	OR, 0.70 (0.28-1.76)
Time to target temperature – hr			
Median (IQR)	5.4 (2.9-8.6)	4.7 (2.6-7.5)	
Geometric mean (95% CI)	6.5 (5.9-7.1)	5.5 (5.0-6.0)	1.19 (1.04-1.36)
Duration of inotropic/catecholamine support – days			
Median (IQR)	1.7 (1.1-2.7)	1.9 (1.2-2.7)	
Geometric mean (95% CI)	1.6 (1.4-1.8)	1.7 (1.5-1.9)	0.94 (0.79-1.12)
Duration of mechanical ventilation – days			
Median (IQR)	2.3 (1.4-4.1)	2.2 (1.5-4.1)	
Geometric mean (95% CI)	2.3 (2.0-2.6)	2.4 (2.1-2.7)	0.96 (0.80-1.14)

* The delayed angiography group is used as the reference group for odds ratios and mean differences.

Secondary end points

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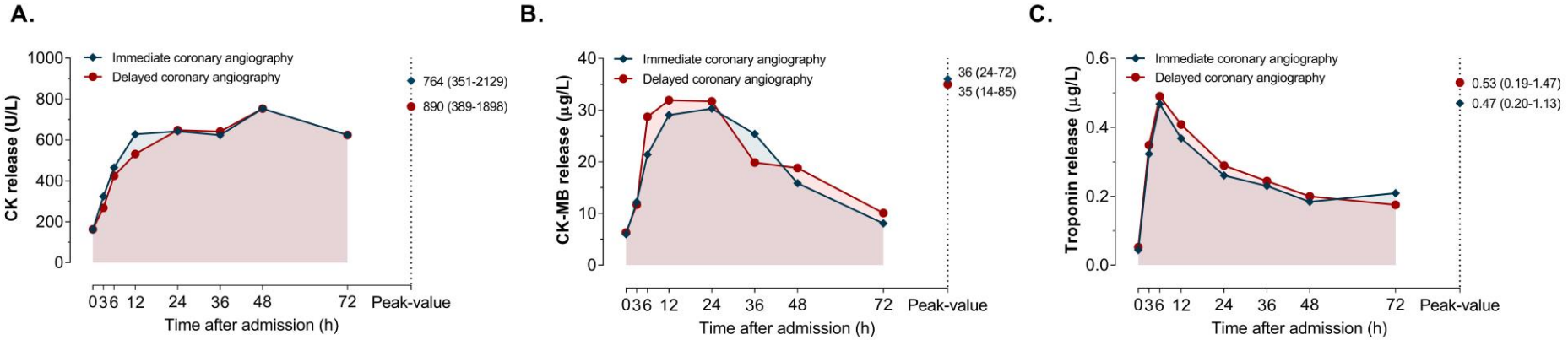
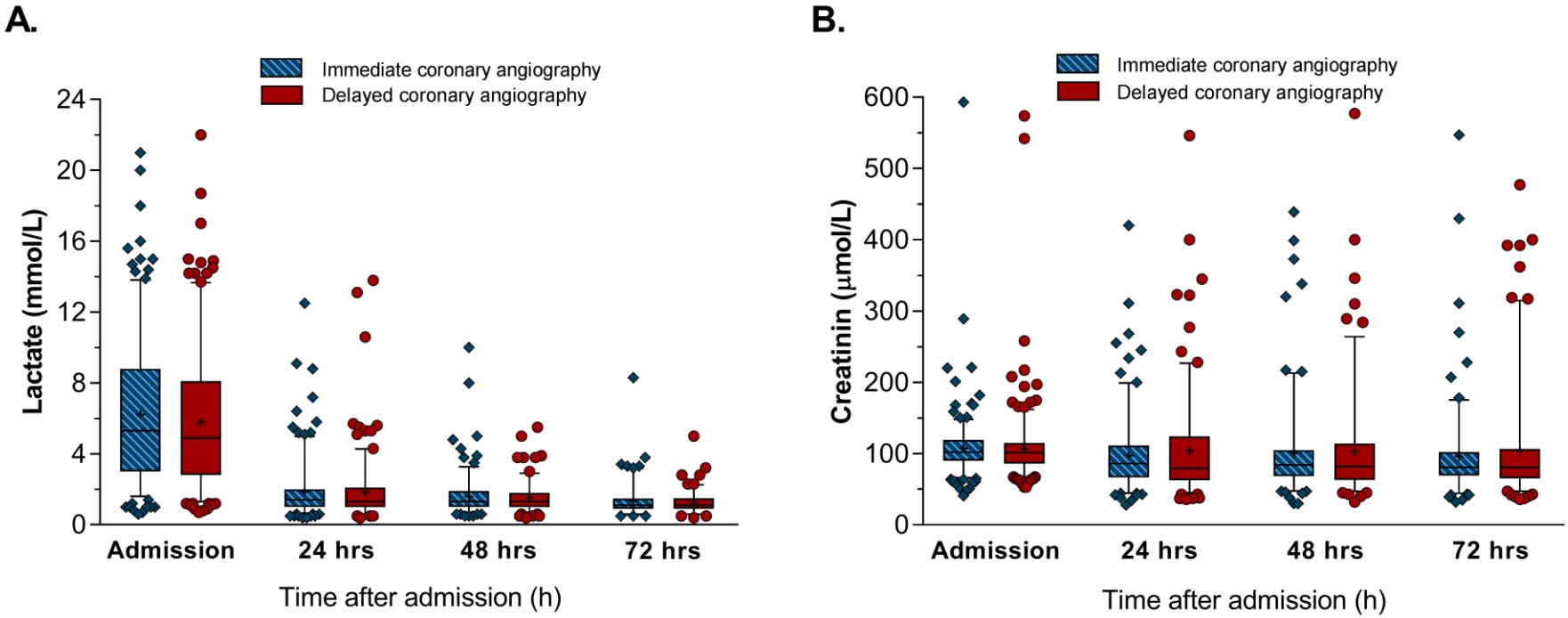
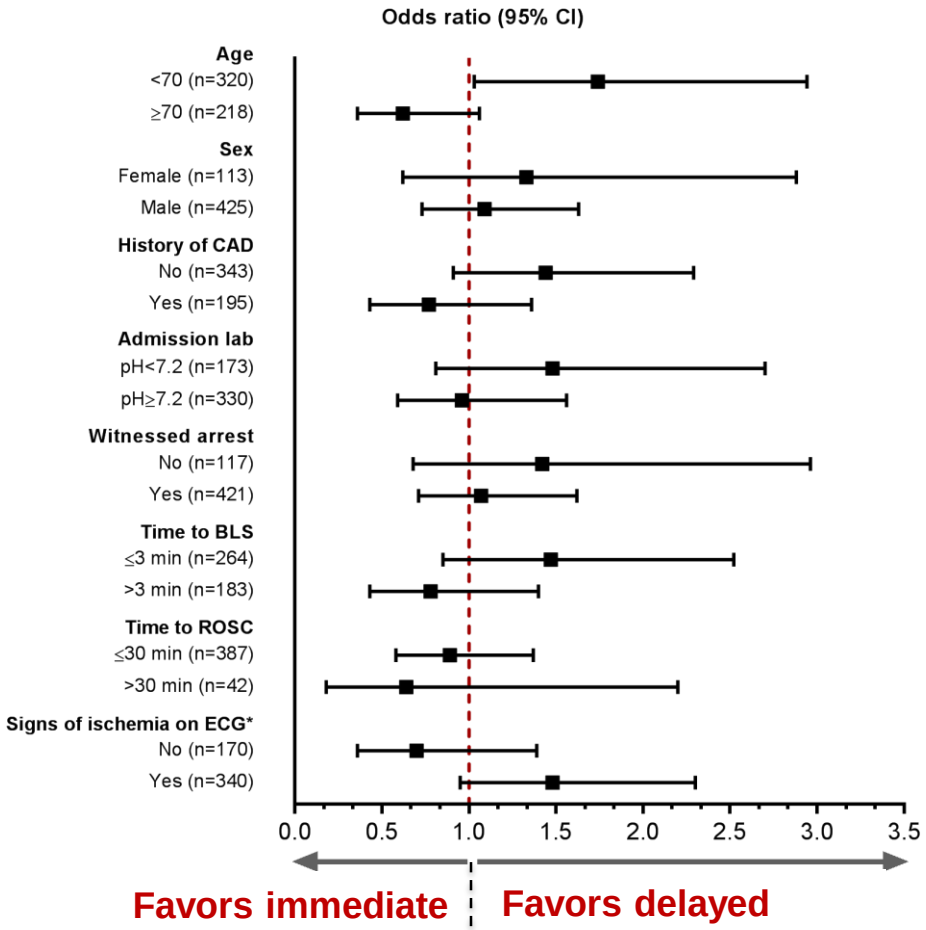
CK, CK-MB and troponin



Lactate and creatinin

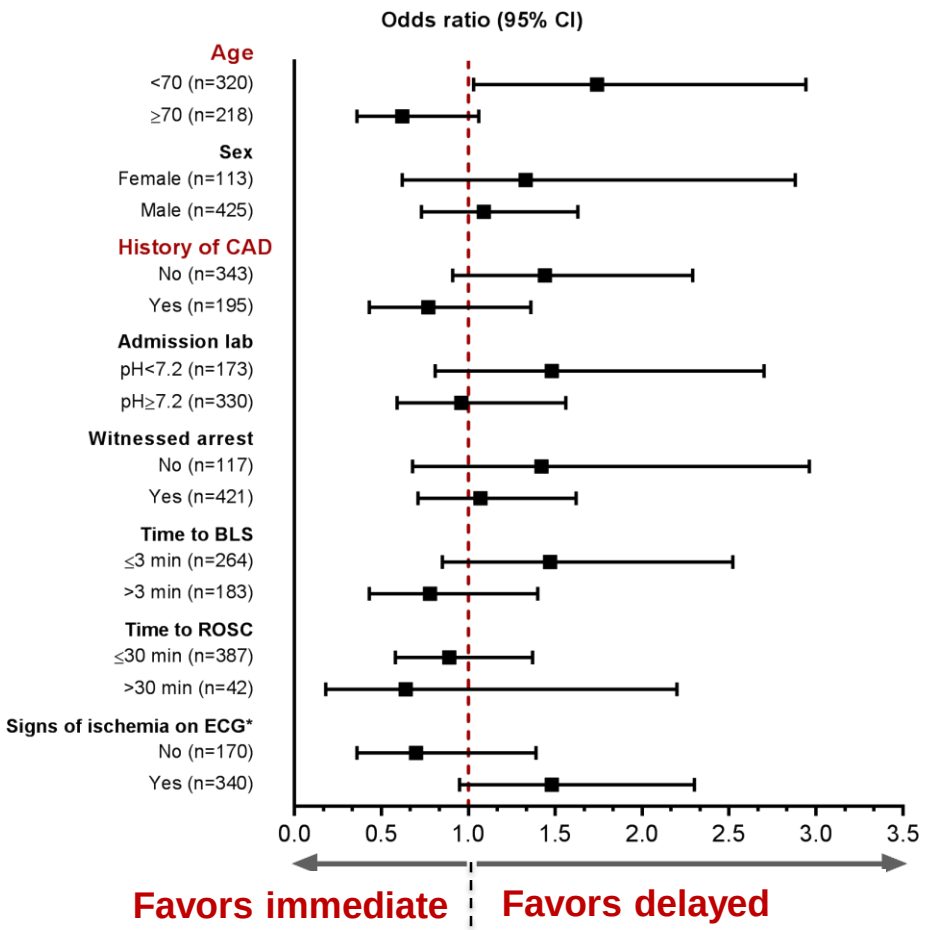


Subgroup analysis



	Odds ratio (95% CI)	No. survival (%) Immediate	No. survival (%) Delayed	*P* Value for Interaction
Age				
<70 (n=320)	1.74 (1.03-2.94)	110 (71.4)	135 (81.3)	0.007
≥70 (n=218)	0.62 (0.36-1.06)	66 (55.5)	43 (43.4)	
Sex				
Female (n=113)	1.33 (0.62-2.88)	30.0 (60.0)	42 (66.7)	0.65
Male (n=425)	1.09 (0.73-1.63)	146 (65.5)	136 (67.3)	
History of CAD				
No (n=343)	1.44 (0.91-2.29)	113 (64.9)	123 (72.8)	0.009
Yes (n=195)	0.77 (0.43-1.36)	63 (63.6)	55 (57.3)	
Admission lab				
pH<7.2 (n=173)	1.48 (0.81-2.70)	40 (44.9)	46 (54.8)	0.27
pH≥7.2 (n=330)	0.96 (0.59-1.56)	121 (73.8)	121 (72.9)	
Witnessed arrest				
No (n=117)	1.42 (0.68-2.96)	29 (52.7)	38 (61.3)	0.52
Yes (n=421)	1.07 (0.71-1.62)	147 (67.4)	140 (69.0)	
Time to BLS				
≤3 min (n=264)	1.47 (0.85-2.52)	93 (67.9)	96 (75.6)	0.12
>3 min (n=183)	0.78 (0.43-1.40)	53 (58.9)	49 (52.7)	
Time to ROSC				
≤30 min (n=387)	0.89 (0.58-1.37)	138 (69.7)	127 (67.2)	0.62
>30 min (n=42)	0.64 (0.18-2.20)	11 (47.8)	7 (36.8)	
Signs of ischemia on ECG*				
No (n=170)	0.70 (0.36-1.39)	72 (76.6)	53 (69.7)	0.07
Yes (n=340)	1.48 (0.95-2.30)	97 (57.7)	115 (66.9)	

Subgroup analysis



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Conclusion

- In patients with ROSC after OHCA without signs of STEMI, immediate coronary angiography was not found to improve survival at 90 days compared to delayed coronary angiography.

- Patients allocated to immediate coronary angiography reached their target temperature later as compared to delayed coronary angiography.

- There was no significant difference in myocardial injury between the two treatment groups.

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ORIGINAL ARTICLE

Coronary Angiography after Cardiac Arrest without ST-Segment Elevation

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