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Case study #1

Evolving Concepts in Non-ST Elevation ACS (NSTE-ACS)

Fernando Bátiz MD

PGY-5 cardiology fellow

Hospital Español

Fernando Bátiz
fernando_batiz@me.com

Sex: Female

Race: Caucasian

Age: 79 years old

CC: chest pain

Fernando Bátiz
fernando_batiz@me.com

Family history

None

Social history

3 cigarettes per day for 30 years

Fernando Bátiz
fernando_batiz@me.com

Past medical & surgical history

1953 Appendectomy

Unspecified chronic joint pain

Meds:

NSAIDs PRN for joint pain

Fernando Bátiz
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HPI

79 year old female patient that presented to our ED complaining of sudden onset of oppressive chest pain 7/10 in intensity that radiated to the left arm. It presented 3 hours before ED eval and lasted for 1 hour. It was not associated with exertion. Her discomfort was associated by nausea and profuse sweating. Asymptomatic in ED. When asked, she had a similar episode 1 week ago.

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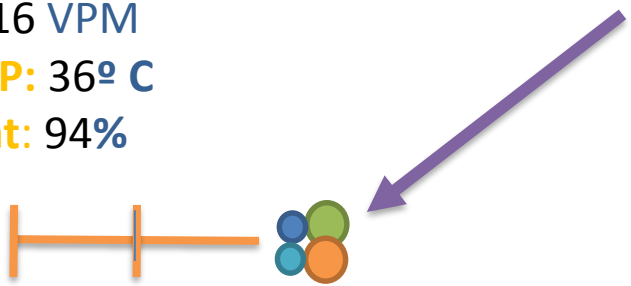
Physical examination

BP: 140/80 mmHg
HR: 70 BPM
RR: 16 VPM
TEMP: 36º C
O_2Sat: 94%



Ø murmurs, S3, S4 or rubs.

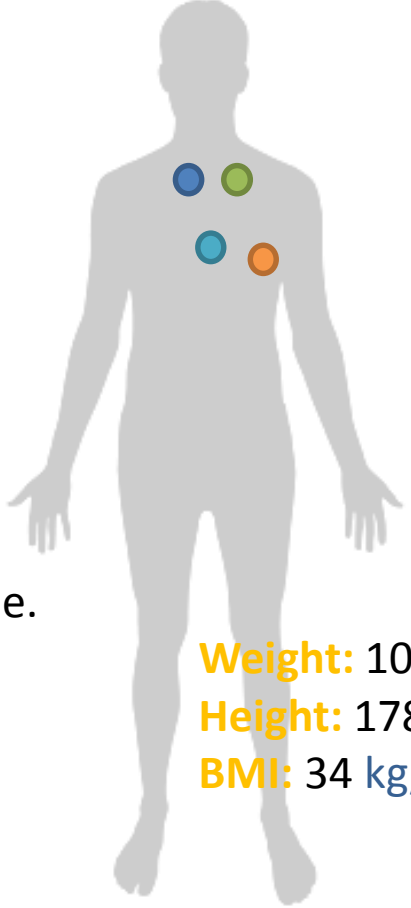
Neck: Ø JVD

Heart:

Chest: Unremarkable.

Abdomen: Unremarkable.

Extremities: Ø edema.



Weight: 107 Kg
Height: 178 cm
BMI: 34 kg/m^2

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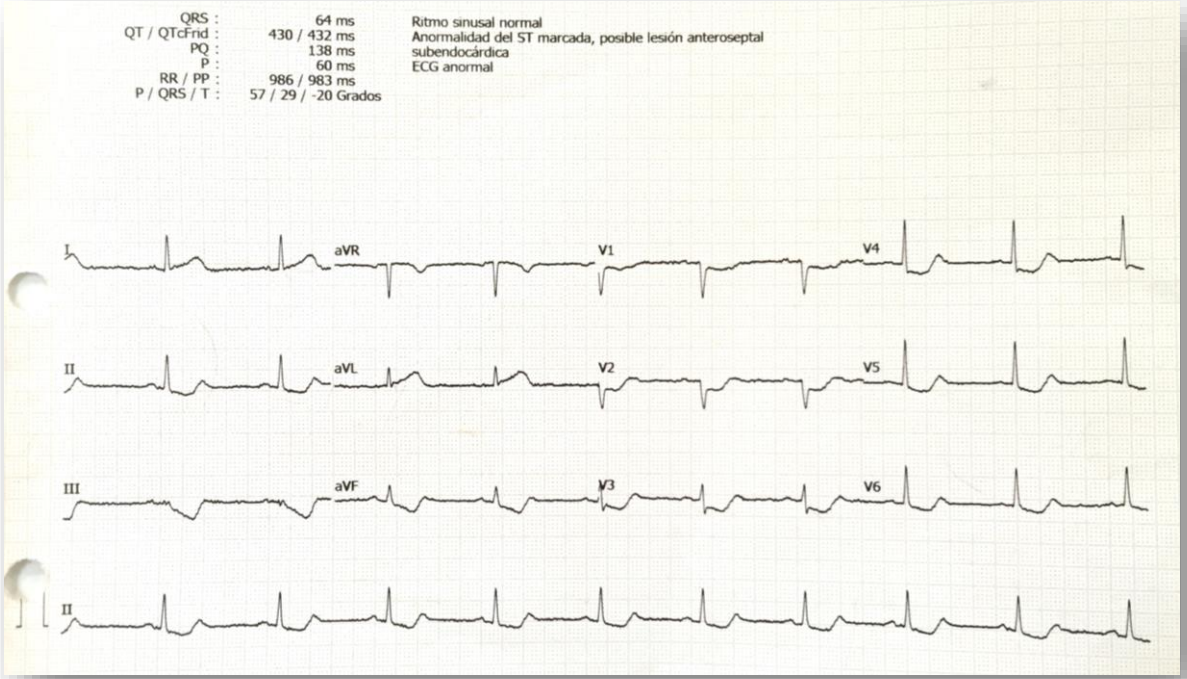

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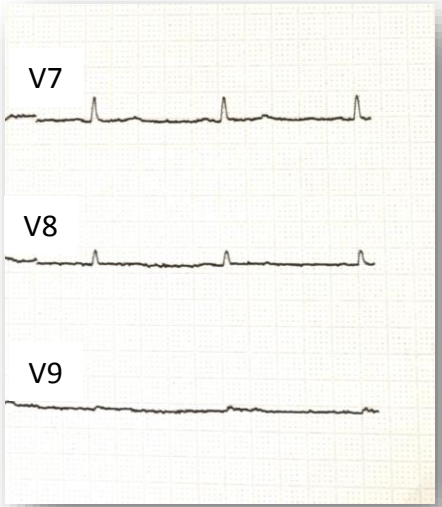
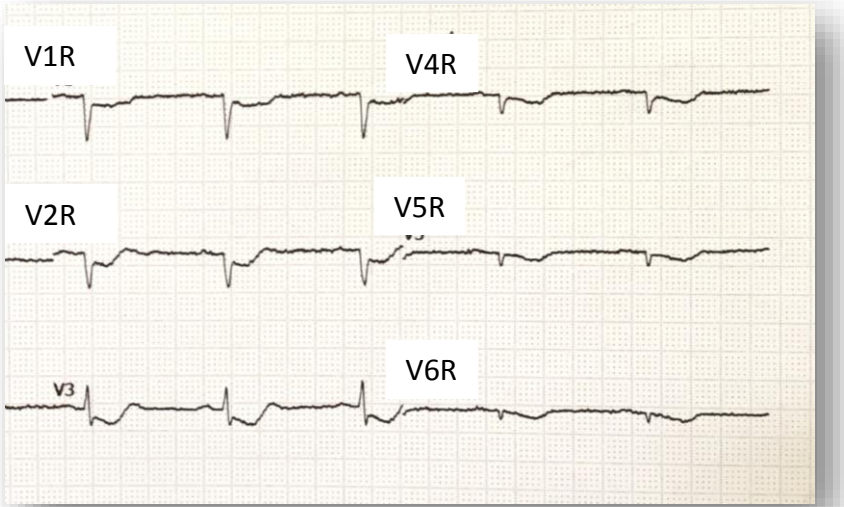
Posterior leads



Right leads



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ER LABS

CE	
Troponin I	0.05 ng/dL
Myoglobin	47 mg/dL
CK	84 mg/dL
CKMB	2.5 mg/dL

CBC	
Leuk	6.4x103/uL
Hb	17.2g/dL
PLT	243x103/uL
Neut	4.85x103/uL
Lymph	1.6x103/mL

BMP	
Na	136mmol/L
K	4mmol/L
Cl	102mmol/L
CO_2	22.3mmol/L
Mg	1.97mg/dL
Creatinine	0.7 mg/dL
BUN	24.02mg/dL
Uric acid	3.88mg/dL
Urea	24.6mg/dL
$HbA1_c$	5.8%

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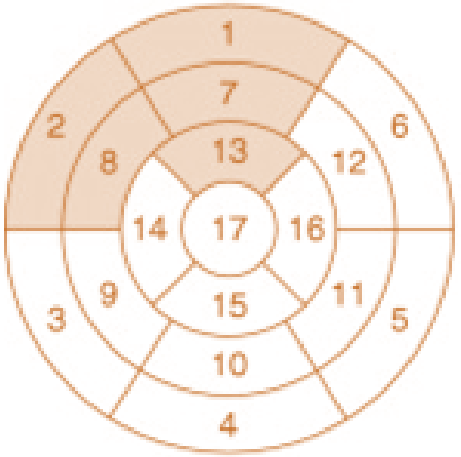
GE Healthcare
Vscan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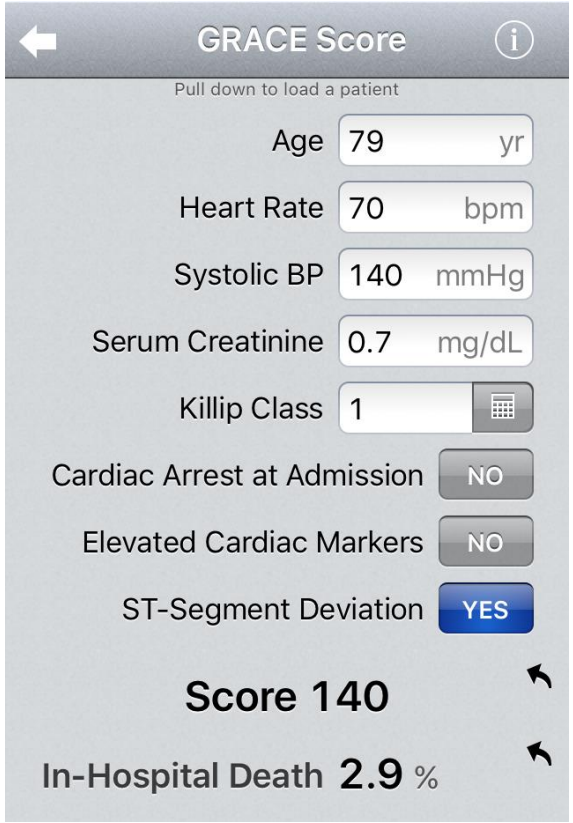

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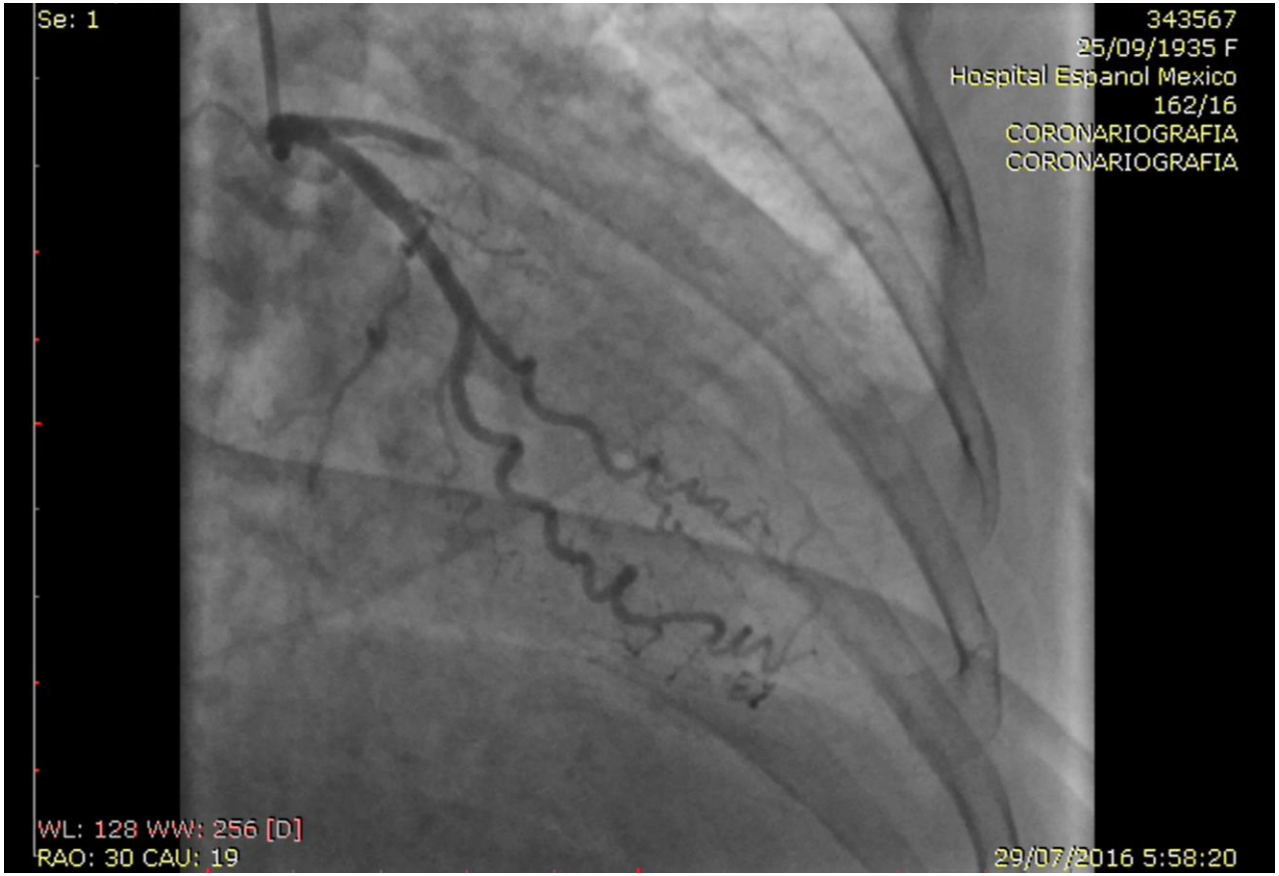
ARS Question:Which type of invasive strategy would you choose for this patient?

Immediate <2hrs	Early <24hrs	Delayed 25-72hrs
1	2	3

She was admitted to the CCU and was eventually (4 hours later) taken to the cathlab.

Ticagrelor 180mg
Aspirin 250mg



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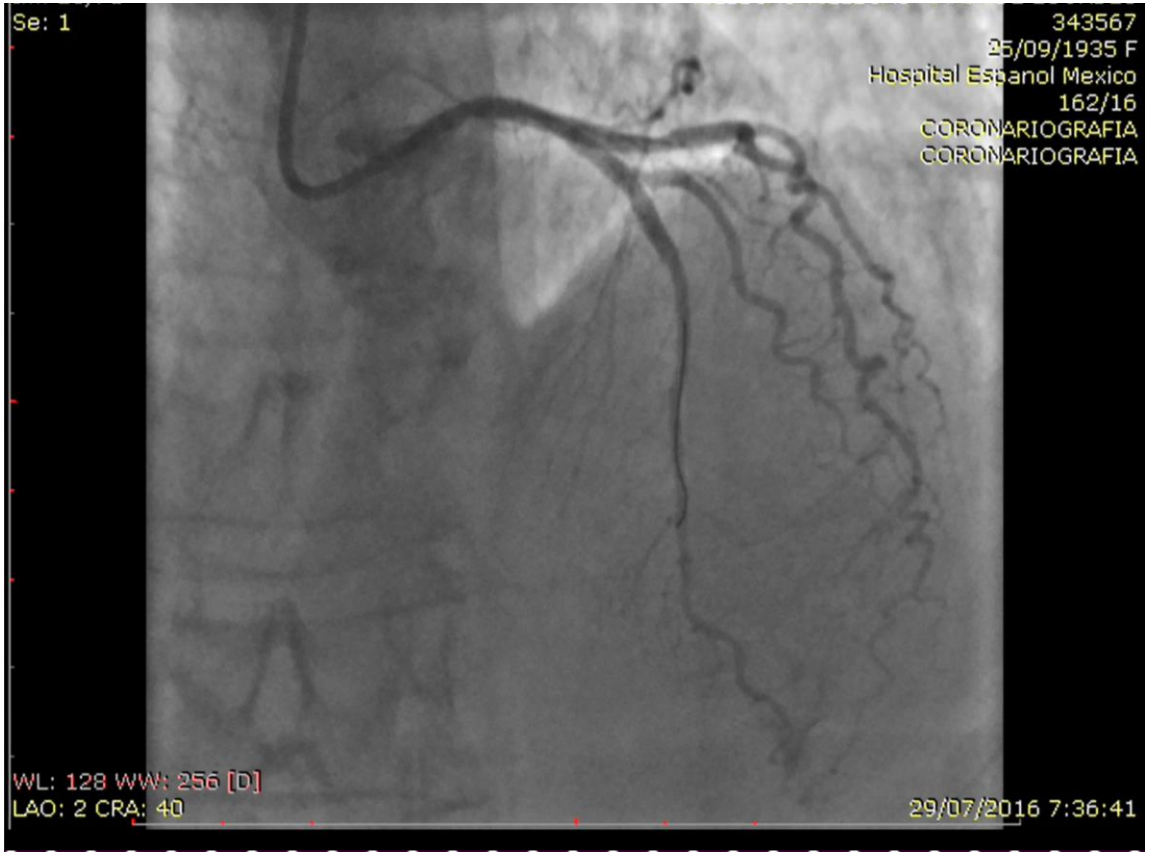

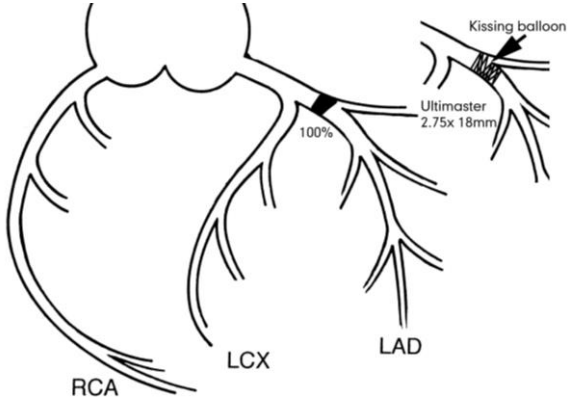

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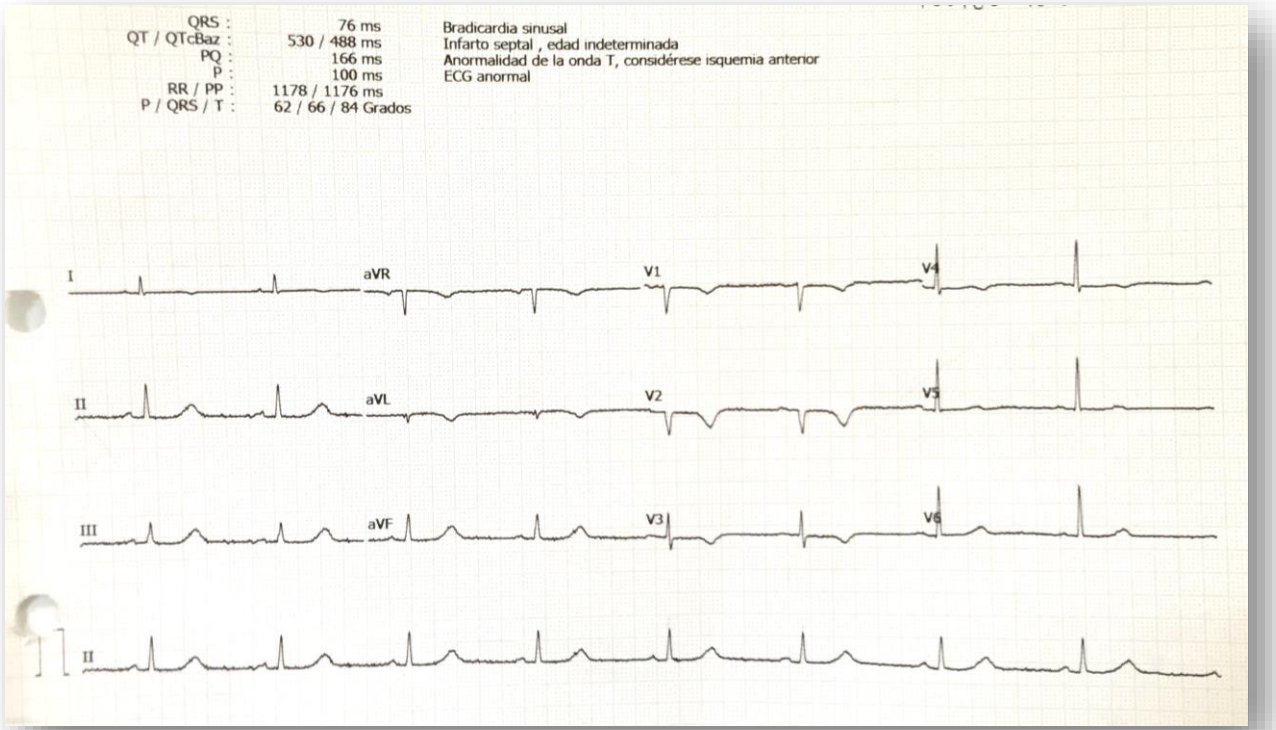
Post PCI



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Early versus delayed invasive strategies

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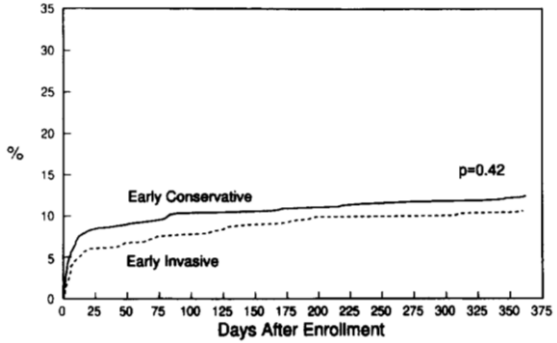
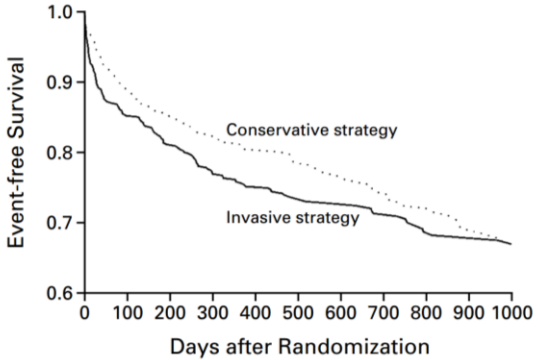
TIMI IIIB



1 YEAR

VANQWISH



AVG FU 23MO

Anderson HV, Cannon CP, Stone PH, et al. One-year results of the thrombolysis in myocardial infarction (TIMI) IIIB clinical trial. A randomized comparison of tissue-type plasminogen activator versus placebo and early invasive versus early conservative strategies in unstable angina and non-Q wave Myocardial infarction. *J Am Coll Cardiol*. 1995;26(7):1643-1650.

Boden WE, O'rourke R a., Crawford MH, et al. Outcomes in Patients with Acute Non-Q-Wave Myocardial Infarction Randomly Assigned to an Invasive as Compared with a Conservative Management Strategy. *N* Engl J Med 1998 Oct 8;339(15):1091.

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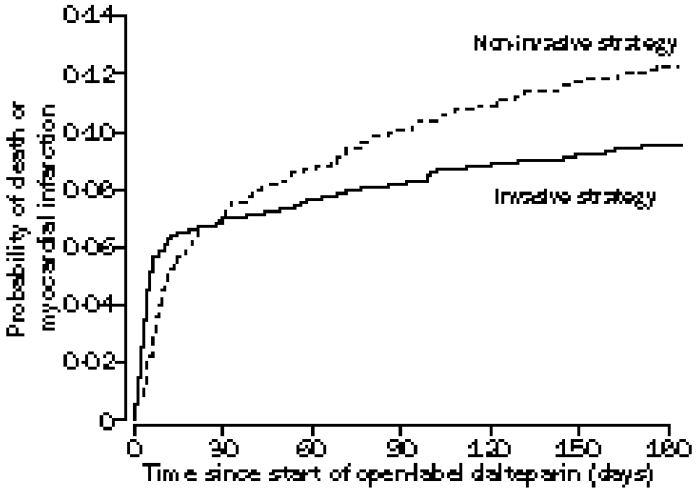
FRISC II



6MO

(Risk ratio 0.78 [95% CI 0.62–0.98], p=0.031)

	Invasive (n=1207)	Non-invasive (n=1226)	Risk ratio (95% CI)	p
Death, MI, or both*	113 (9·4%)	148 (12·1%)	0·78 (0·62–0·98)	0·031
MI	94 (7·8%)	124 (10·1%)	0·77 (0·60–0·99)	0·045
Death	23 (1·9%)	36 (2·9%)	0·65 (0·39–1·09)	0·10

MI=myocardial infarction.
*In invasive group, six (0·5%) of events occurred before randomised revascularisation procedure.

Ragmin F. Invasive compared with non-invasive treatment in unstable coronary-artery disease: FRISC II prospective randomized multicentre study. *Lancet*. 1999;354(9180):708-715.

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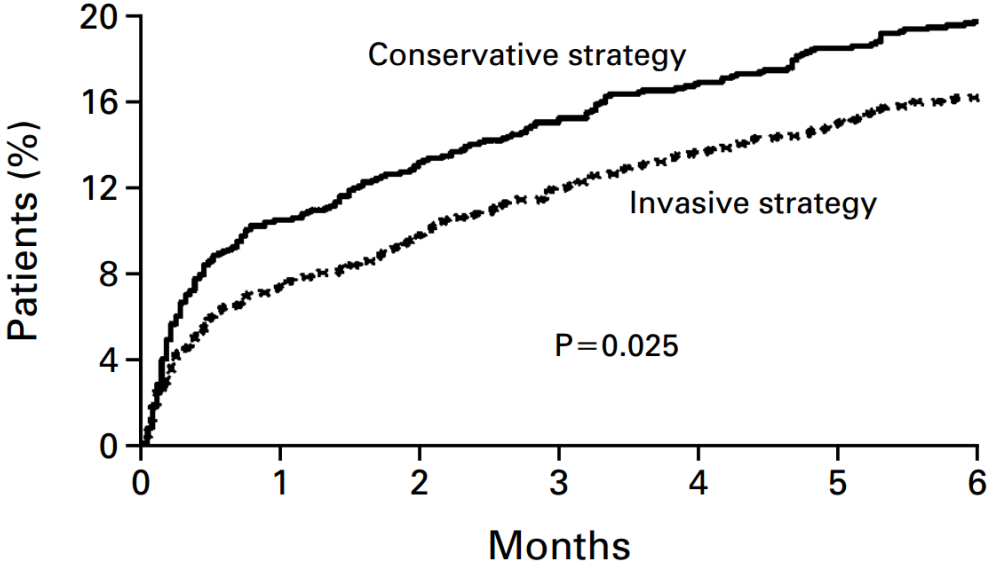
TACTICS TIMI 18



Primary endopoint:

Death, Nonfatal Myocardial Infarction, or Rehospitalization for an Acute Coronary Syndrome during the Six-Month Follow-up Period.

Cannon CP, Weintraub WS, Demopoulos LA, et al. Comparison of Early Invasive and Conservative Strategies in Patients with Unstable Coronary Syndromes Treated with the Glycoprotein IIb/IIIa Inhibitor Tirofiban. *N Engl J Med*. 2001;344(25):1879-1887.

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CLINICAL PRACTICE GUIDELINE

2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes

Several studies (93,138,334-337) and meta-analyses (141,340) have concluded that a strategy of routine invasive therapy is generally superior to an ischemia-guided strategy or selectively invasive approach. One study reported that the routine invasive strategy resulted in an 18% relative reduction in death or MI, including a significant reduction in MI alone (341). The routine invasive arm was associated with higher in-hospital mortality (1.8% versus 1.1%), but this disadvantage was more than compensated for by a significant reduction in mortality between discharge and the end of follow-up (3.8% versus 4.9%). The invasive strategy was also

Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC guideline for the management of patients with Non-ST-Elevation acute coronary syndromes: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014

Timing…

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ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2014.09.017

CLINICAL PRACTICE GUIDELINE

2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the Society for Cardiovascular Angiography and Interventions and Society of Thoracic Surgeons

Endorsed by the American Association for Clinical Chemistry

Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC guideline for the management of patients with Non-ST-Elevation acute coronary syndromes: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014

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TABLE 8 Factors Associated With Appropriate Selection of Early Invasive Strategy or Ischemia-Guided Strategy in Patients With NSTE-ACS

Immediate invasive (within 2 h)	Refractory angina
	Signs or symptoms of HF or new or worsening mitral regurgitation
	Hemodynamic instability
	Recurrent angina or ischemia at rest or with low-level activities despite intensive medical therapy
	Sustained VT or VF
Ischemia-guided strategy	Low-risk score (e.g., TIMI [0 or 1], GRACE [<109])
	Low-risk Tn-negative female patients
	Patient or clinician preference in the absence of high-risk features
Early invasive (within 24 h)	None of the above, but GRACE risk score >140
	Temporal change in Tn (Section 3.4)
	New or presumably new ST depression
Delayed invasive (within 25–72 h)	None of the above but diabetes mellitus
	Renal insufficiency (GFR <60 mL/min/1.73 m^2)
	Reduced LV systolic function (EF <0.40)
	Early postinfarction angina
	PCI within 6 mo
	Prior CABG
	GRACE risk score 109-140; TIMI score ≥2

Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC guideline for the management of patients with Non-ST-Elevation acute coronary syndromes: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014

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CLASS I

1. An urgent/immediate invasive strategy (diagnostic angiography with intent to perform revascularization if appropriate based on coronary anatomy) is indicated in patients (men and women[¶]) with NSTE-ACS who have refractory angina or hemodynamic or electrical instability (without serious comorbidities or contraindications to such procedures) (42,44,138,338). *(Level of Evidence: A)*

2. An early invasive strategy (diagnostic angiography with intent to perform revascularization if appropriate based on coronary anatomy) is indicated in initially stabilized patients with NSTE-ACS (without serious comorbidities or contraindications to such procedures) who have an elevated risk for clinical events (Table 8) (42,44,138,333,334,338,339). *(Level of Evidence: B)*

TABLE 8 Factors Associated With Appropriate Selection of Early Invasive Strategy or Ischemia-Guided Strategy in Patients With NSTE-ACS

Immediate invasive (within 2 h)	Refractory angina
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	PCI within 6 mo
	Prior CABG
	GRACE risk score 109-140; TIMI score ≥2

Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC guideline for the management of patients with Non-ST-Elevation acute coronary syndromes: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014

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CLASS III: NO BENEFIT

1. An early invasive strategy (i.e., diagnostic angiography with intent to perform revascularization) is not recommended in patients with:
   a. Extensive comorbidities (e.g., hepatic, renal, pulmonary failure; cancer), in whom the risks of revascularization and comorbid conditions are likely to outweigh the benefits of revascularization. *(Level of Evidence: C)*
   b. Acute chest pain and a low likelihood of ACS who are troponin-negative *(Level of Evidence: C)*, especially women (141). *(Level of Evidence: B)*

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	Patient or clinician preference in the absence of high-risk features
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	PCI within 6 mo
	Prior CABG
	GRACE risk score 109-140; TIMI score ≥2

Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC guideline for the management of patients with Non-ST-Elevation acute coronary syndromes: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014

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European Heart Journal
doi:10.1093/eurheartj/ehv320

ESC GUIDELINES

2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC)

Roffi M, Patrono C, Collet J-P, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J*. 2015

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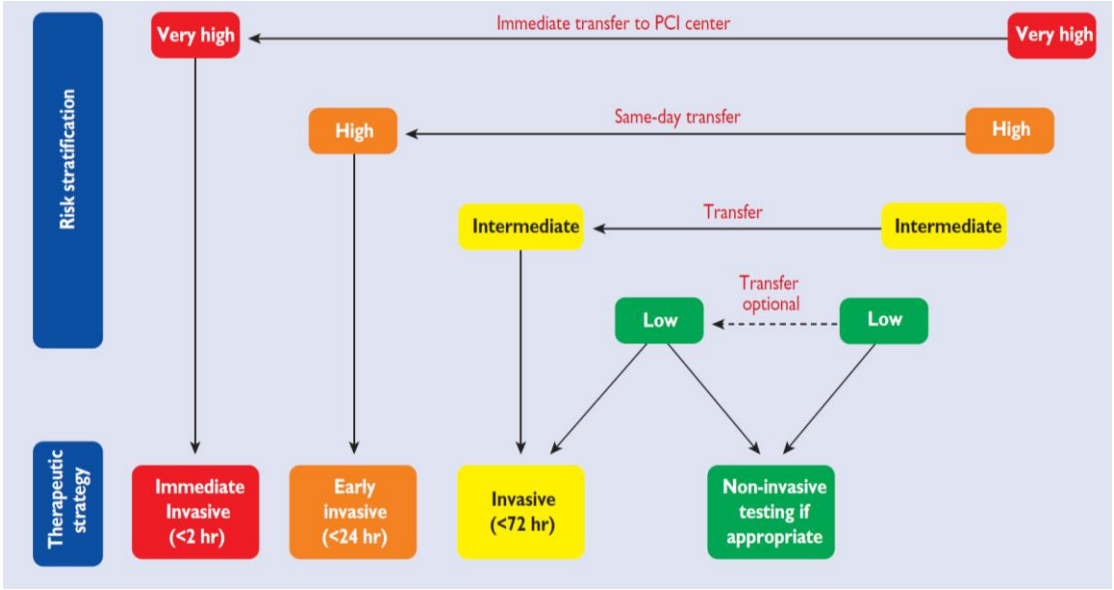
Table 13 Risk criteria mandating invasive strategy in NSTE-ACS

Very-high-risk criteria
• Haemodynamic instability or cardiogenic shock
• Recurrent or ongoing chest pain refractory to medical treatment
• Life-threatening arrhythmias or cardiac arrest
• Mechanical complications of MI
• Acute heart failure
• Recurrent dynamic ST-T wave changes, particularly with intermittent ST-elevation
High-risk criteria
• Rise or fall in cardiac troponin compatible with MI
• Dynamic ST- or T-wave changes (symptomatic or silent)
• GRACE score >140
Intermediate-risk criteria
• Diabetes mellitus
• Renal insufficiency (eGFR <60 mL/min/1.73 m²)
• LVEF <40% or congestive heart failure
• Early post-infarction angina
• Prior PCI
• Prior CABG
• GRACE risk score >109 and <140
Low-risk criteria
• Any characteristics not mentioned above



Roffi M, Patrono C, Collet J-P, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J*. 2015

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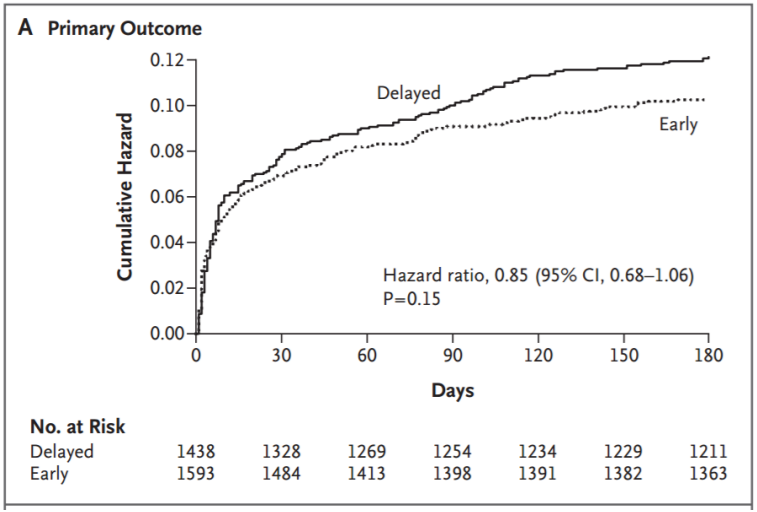
TIMACS

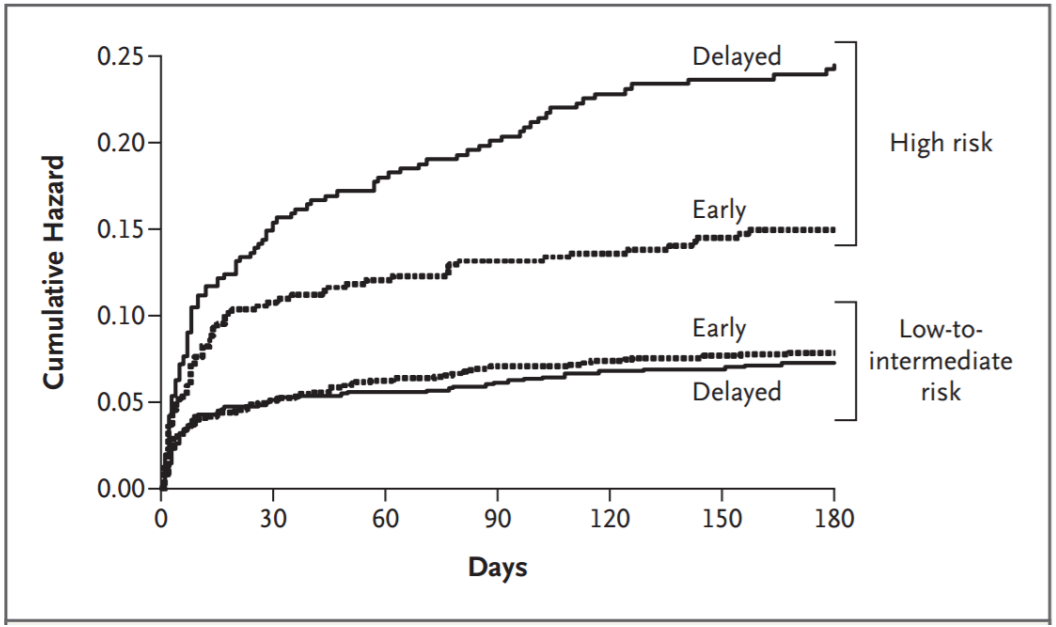


Composite of death, myocardial infarction, or stroke at 6 months

Early intervention did not differ greatly from delayed intervention in preventing the primary outcome.

Mehta SR, Granger CB, Boden WE, et al. Early versus Delayed Invasive Intervention in Acute Coronary Syndromes. *N Engl J Med*. 2009;360(21):2165-2175.

TIMACS



Grace >140

Grace ≤140

Mehta SR, Granger CB, Boden WE, et al. Early versus Delayed Invasive Intervention in Acute Coronary Syndromes. *N Engl J Med*. 2009;360(21):2165-2175.

TIMACS

Secondary outcome

Secondary outcome

Table 2. Primary and Secondary Outcomes.*

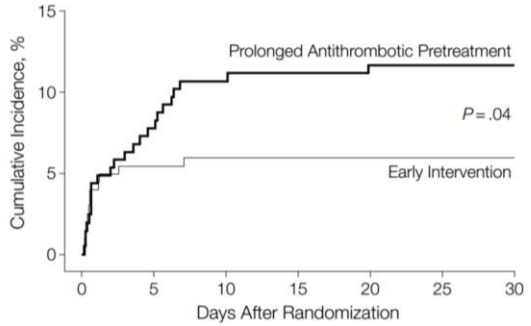
Variable	Early Intervention (N=1593)	Delayed Intervention (N=1438)	Hazard Ratio (95% CI)	P Value
	percent			
At 6 mo				
Death, myocardial infarction, or stroke	9.6	11.3	0.85 (0.68–1.06)	0.15
Death, myocardial infarction, or refractory ischemia	9.5	12.9	0.72 (0.58–0.89)	0.003
Death, myocardial infarction, stroke, refractory ischemia, or repeat intervention	16.6	19.5	0.84 (0.71–0.99)	0.04
Death	4.8	5.9	0.81 (0.60–1.11)	0.19
Myocardial infarction	4.8	5.7	0.83 (0.61–1.14)	0.25
Stroke	1.3	1.4	0.90 (0.49–1.68)	0.74
Refractory ischemia	1.0	3.3	0.30 (0.17–0.54)	<0.001
Repeat intervention	8.7	8.5	1.04 (0.82–1.34)	0.73
At 30 days				
Death, myocardial infarction, or stroke	6.7	7.6	0.88 (0.67–1.15)	0.34
Death, myocardial infarction, or refractory ischemia	6.6	9.3	0.70 (0.54–0.90)	0.006
Death, myocardial infarction, stroke, refractory ischemia, or repeat intervention	12.0	13.0	0.91 (0.75–1.12)	0.37
Death	2.9	3.3	0.86 (0.58–1.29)	0.48
Myocardial infarction	3.6	4.1	0.87 (0.61–1.25)	0.46
Stroke	0.9	0.9	1.04 (0.50–2.19)	0.91
Refractory ischemia	1.0	3.1	0.30 (0.17–0.55)	<0.001
Repeat intervention	5.9	4.2	1.39 (1.01–1.93)	0.05

Mehta SR, Granger CB, Boden WE, et al. Early versus Delayed Invasive Intervention in Acute Coronary Syndromes. *N Engl J Med*. 2009;360(21):2165-2175.

Security

ISAR COOL

Figure 3. Cumulative Incidence of Death and Myocardial Infarction at 30 Days



No. at Risk							
Prolonged Antithrombotic Pretreatment	207	191	185	184	183	183	183
Early Intervention	203	192	191	191	191	191	191

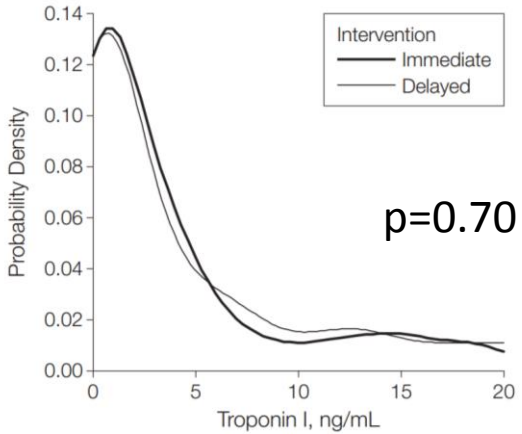
Conclusion In patients with unstable coronary syndromes, deferral of intervention for prolonged antithrombotic pretreatment does not improve the outcome compared with immediate intervention accompanied by intense antiplatelet treatment.

JAMA. 2003;290:1593-1599 www.jama.com

Neumann F, Kastrati A, Pogatsa-Murray G, al et. Evaluation of prolonged antithrombotic pretreatment ("cooling-off" strategy) before intervention in patients with unstable coronary syndromes: A randomized controlled trial. *JAMA*. 2003;290(12):1593-1599.

ABOARD

Figure 2. Peak Troponin I Values (Primary End Point) in Groups Receiving Immediate and Delayed Invasive Intervention



Median troponin I value

N = 352

Immediate		Delayed
2.1 [0.3- 7.1] ng/mL	VS	1.7 [0.3-7.2] ng/mL

Montalescot G, Cayla G, Collet JP, et al. Immediate vs delayed intervention for acute coronary syndromes: a randomized clinical trial. JAMA 2009;302:947–54.

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European Heart Journal (2011) **32**, 32–40
doi:10.1093/eurheartj/ehq276

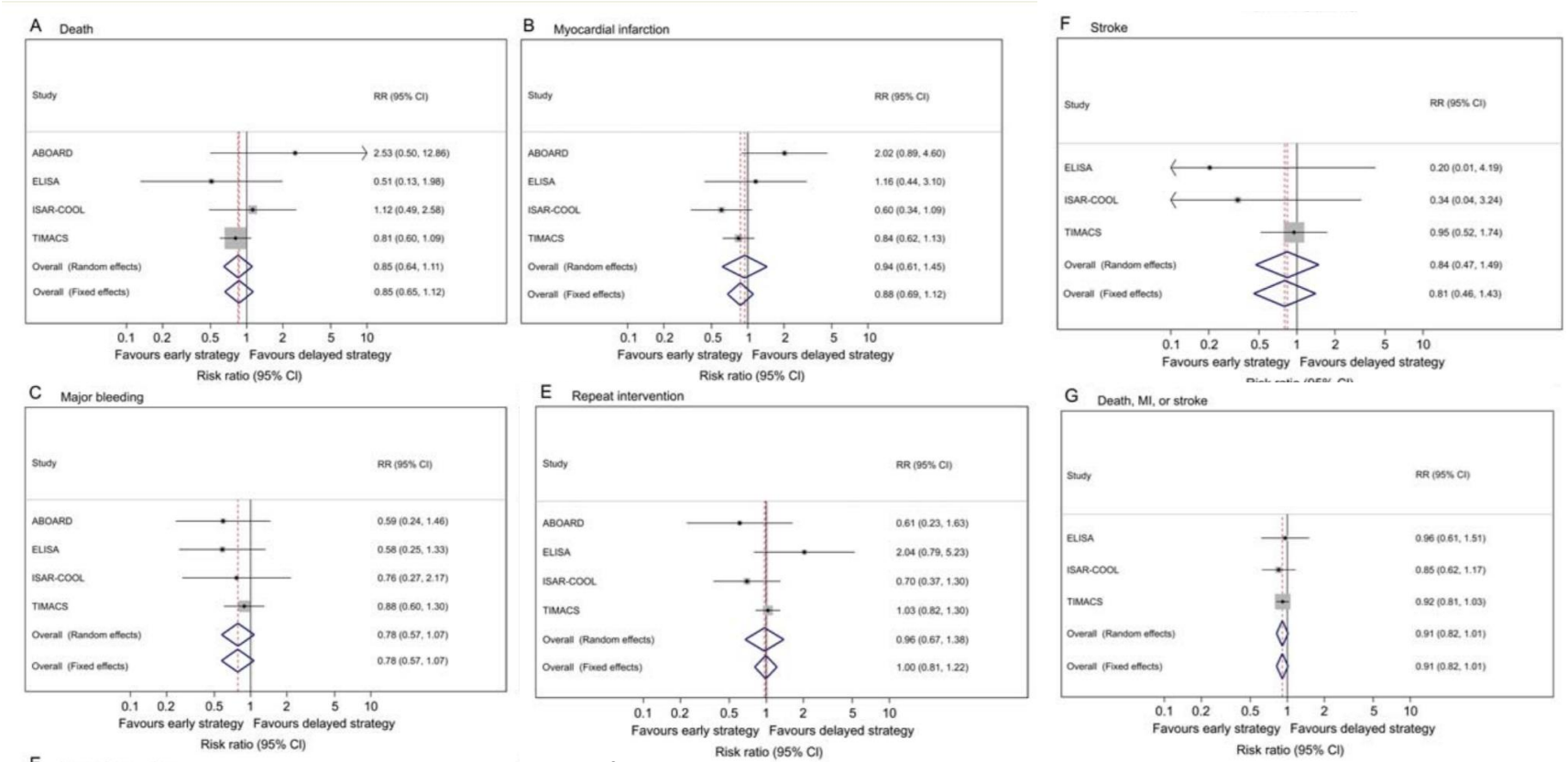
CLINICAL RESEARCH
Coronary heart disease

Optimal timing of coronary angiography and potential intervention in non-ST-elevation acute coronary syndromes

Demosthenes G. Katritsis[1]*, George C.M. Siontis[2], Adnan Kastrati[3], Arnoud W.J. van't Hof[4], Franz-Josef Neumann[3], Konstantinos C.M. Siontis[2], and John P.A. Ioannidis[2,5,6]

N: 4 RCT → N: 4´013

Katritsis DG, Siontis GCM, Kastrati A, et al. Optimal timing of coronary angiography and potential intervention in non-ST-elevation acute coronary syndromes. *Eur Heart J*. 2011;32(1):32-40.



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Annals of Internal Medicine | Review

Optimal Timing of Coronary Invasive Strategy in Non–ST-Segment Elevation Acute Coronary Syndromes

A Systematic Review and Meta-analysis

Eliano P. Navarese, MD, PhD; Paul A. Gurbel, MD; Felicita Andreotti, MD, PhD; Udaya Tantry, PhD; Young-Hoon Jeong, MD, PhD; Marek Kozinski, MD, PhD; Thomas Engstrøm, MD; Giuseppe Di Pasquale, MD; Waclaw Kochman, MD; Diego Ardissino, MD; Elvin Kedhi, MD; Gregg W. Stone, MD; and Jacek Kubica, MD, PhD

N: 7 RCT
4 Observational studies → N: 77´499

Navarese EP, Gurbel PA, Andreotti F, et al. Optimal Timing of Coronary Invasive Strategy in Non–ST-Segment Elevation Acute Coronary Syndromes A Systematic Review and Meta-analysis. *Ann Intern Med*. 2013;158(4):261-270.

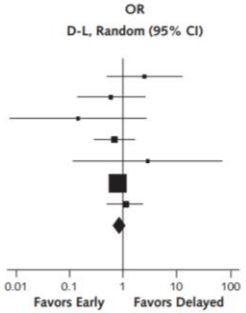
Figure 1. **Individual and summary ORs for mortality in randomized trials and observational studies comparing early versus delayed intervention.**

Randomized Trials

Study or Subgroup	Early Strategy Events, *n*	Early Strategy Total Patients, *n*	Delayed Strategy Events, *n*	Delayed Strategy Total Patients, *n*	Weight, %	OR D-L, Random (95% CI)
ABOARD	5	175	2	177	2.6	2.57 (0.49–13.45)
ELISA	3	109	5	111	3.4	0.60 (0.14–2.57)
ISAR-COOL	0	203	3	207	0.8	0.14 (0.01–2.80)
LIPSIA-NSTEMI	9	200	13	200	9.4	0.68 (0.28–1.62)
OPTIMA	1	73	0	69	0.7	2.88 (0.12–71.80)
TIMACS	76	1593	85	1438	70.8	0.80 (0.58–1.10)
Zhang et al, 2010 (16)	16	446	12	369	12.3	1.11 (0.52–2.37)
Total	110	2799	120	2571	100	0.83 (0.64–1.09)

Heterogeneity: $\tau^2 = 0.00$; chi-square = 4.72; $P = 0.58$; $I^2 = 0\%$

Test for overall effect: $Z = 1.36$ ($P = 0.180$)



Observational Studies

Study or Subgroup	Early Strategy Events, *n*	Early Strategy Total Patients, *n*	Delayed Strategy Events, *n*	Delayed Strategy Total Patients, *n*	Weight, %	OR D-L, Random (95% CI)
ACUITY	123	4937	121	2812	24.2	0.57 (0.44–0.73)
CRUSADE	1867	45 548	475	10 804	31.5	0.93 (0.84–1.03)
GRACE	72	2407	176	4639	23.0	0.78 (0.59–1.03)
SYNERGY	84	3326	77	3026	21.2	0.99 (0.73–1.36)
Total	2146	56 218	849	21 281	100	0.80 (0.63–1.02)

Heterogeneity: $\tau^2 = 0.04$; chi-square = 13.51; $P = 0.004$; $I^2 = 78\%$

Test for overall effect: $Z = 1.79$ ($P = 0.070$)

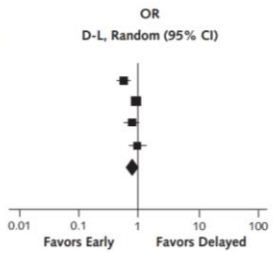


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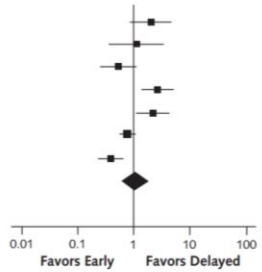
Figure 2. **Individual and summary ORs for myocardial infarction in randomized trials and observational studies comparing early versus delayed intervention.**

Randomized Trials

Study or Subgroup	Early Strategy Events, *n*	Early Strategy Total Patients, *n*	Delayed Strategy Events, *n*	Delayed Strategy Total Patients, *n*	Weight, %	OR D-L, Random (95% CI)
ABOARD	16	175	8	177	12.8	2.13 (0.89–5.10)
ELISA	7	109	6	111	10.6	1.20 (0.39–3.70)
ISAR-COOL	12	203	21	207	14.0	0.56 (0.27–1.16)
LIPSIA-NSTEMI	33	200	13	200	14.6	2.84 (1.45–5.58)
OPTIMA	44	73	27	69	14.6	2.36 (1.20–4.63)
TIMACS	76	1593	82	1438	17.5	0.83 (0.60–1.14)
Zhang et al, 2010 (16)	23	446	40	369	15.9	0.41 (0.24–0.69)
Total	211	2799	197	2541	100	1.15 (0.65–2.01)

Heterogeneity: $\tau^2 = 0.44$; chi-square = 32.98; $P < 0.001$; $I^2 = 82\%$

Test for overall effect: $Z = 0.48$ ($P = 0.63$)

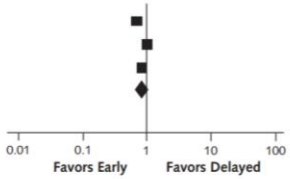


Observational Studies

Study or Subgroup	Early Strategy Events, *n*	Early Strategy Total Patients, *n*	Delayed Strategy Events, *n*	Delayed Strategy Total Patients, *n*	Weight, %	OR D-L, Random (95% CI)
ACUITY	382	4937	301	2812	32.4	0.70 (0.60–0.82)
CRUSADE	1366	45 548	313	10 804	34.5	1.04 (0.91–1.17)
SYNERGY	404	3326	416	3026	33.1	0.87 (0.75–1.00)
Total	2152	53 611	1030	16 642	100	0.86 (0.69–1.08)

Heterogeneity: $\tau^2 = 0.03$; chi-square = 14.66; $P < 0.001$; $I^2 = 86\%$

Test for overall effect: $Z = 1.32$ ($P = 0.190$)



Navarese EP, Gurbel PA, Andreotti F, et al. Optimal Timing of Coronary Invasive Strategy in Non–ST-Segment Elevation Acute Coronary Syndromes A Systematic Review and Meta-analysis. *Ann Intern Med*. 2013;158(4):261-270.

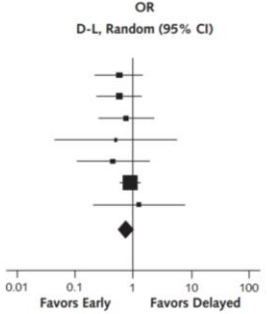
Figure 3. **Individual and summary ORs for major bleeding complications in randomized trials and observational studies comparing early versus delayed intervention.**

Randomized Trials

Study or Subgroup	Early Strategy Events, *n*	Early Strategy Total Patients, *n*	Delayed Strategy Events, *n*	Delayed Strategy Total Patients, *n*	Weight, %	OR D-L, Random (95% CI)
ABOARD	7	175	12	177	10.4	0.57 (0.22–1.49)
ELISA	9	109	15	111	12.5	0.58 (0.24–1.38)
ISAR-COOL	6	203	8	207	8.2	0.76 (0.26–2.22)
LIPSIA-NSTEMI	1	200	2	200	1.6	0.50 (0.04–5.53)
OPTIMA	3	73	6	69	4.7	0.45 (0.11–1.87)
TIMACS	49	1593	50	1438	59.5	0.88 (0.59–1.32)
Zhang et al, 2010 (16)	3	446	2	369	3.0	1.24 (0.21–7.48)
Total	78	2799	95	2571	100	0.76 (0.56–1.04)

Heterogeneity: $\tau^2 = 0.00$; chi-square = 2.17; $P = 0.90$; $I^2 = 0\%$

Test for overall effect: $Z = 1.70$ ($P = 0.090$)

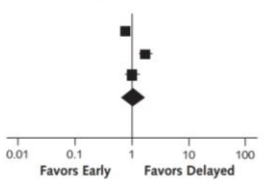


Observational Studies

Study or Subgroup	Early Strategy Events, *n*	Early Strategy Total Patients, *n*	Delayed Strategy Events, *n*	Delayed Strategy Total Patients, *n*	Weight, %	OR D-L, Random (95% CI)
ACUITY	267	4937	191	2812	34.4	0.78 (0.65–0.95)
GRACE	116	2407	130	4639	33.0	1.76 (1.36–2.27)
SYNERGY	113	3326	99	3026	32.6	1.04 (0.79–1.37)
Total	496	10 670	420	10 477	100	1.12 (0.69–1.82)

Heterogeneity: $\tau^2 = 0.17$; chi-square = 24.46; $P < 0.001$; $I^2 = 92\%$

Test for overall effect: $Z = 0.47$ ($P = 0.64$)



Navarese EP, Gurbel PA, Andreotti F, et al. Optimal Timing of Coronary Invasive Strategy in Non–ST-Segment Elevation Acute Coronary Syndromes A Systematic Review and Meta-analysis. *Ann Intern Med*. 2013;158(4):261-270.

Costs

European Heart Journal (2011) 32, 32–40
doi:10.1093/eurheartj/ehq276

CLINICAL RESEARCH
Coronary heart disease

Optimal timing of coronary angiography and potential intervention in non-ST-elevation acute coronary syndromes

Demosthenes G. Katritsis[1]*, George C.M. Siontis[2], Adnan Kastrati[3], Arnoud W.J. van't Hof[4], Franz-Josef Neumann[3], Konstantinos C.M. Siontis[2], and John P.A. Ioannidis[2,5,6]

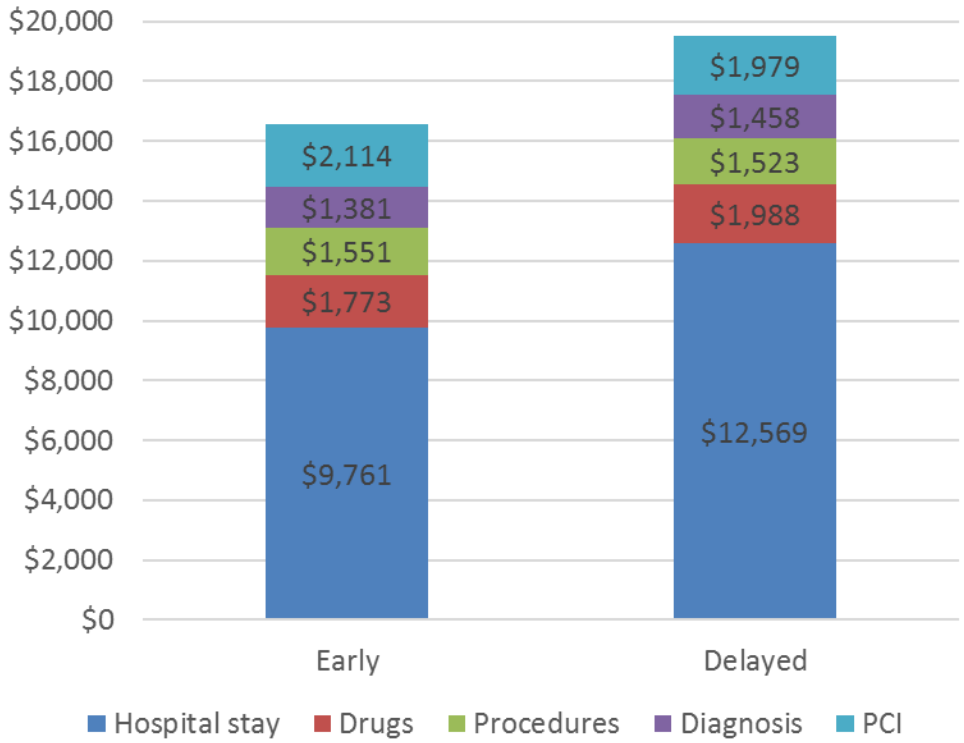
Data on the effects of the two strategies on the duration of hospital stay were reported in three trials (ABOARD, ELISA, ISAR-COOL). Quantitative synthesis of the available data showed a need for shorter hospitalization (by 28%, 95% CI 22–35%, $P < 0.001$; $I^2 = 0\%$) of patients who were randomized to the early strategy compared with those randomized to the delayed strategy.

Table 3 Summary of major clinical outcomes

Outcomes	ABOARD		ELISA		ISAR-COOL		TIMACS	
	Early	Delayed	Early	Delayed	Early	Delayed	Early	Delayed
Death	5 (2.9)	2 (1.1)	3 (2.8)	6 (5.4)	11 (5.4)	10 (4.8)	76 (4.8)	85 (5.9)
MI	16 (9.1)	8 (4.5)	8 (7.3)	7 (6.3)	16 (7.9)	27 (13)	76 (4.8)	82 (5.7)
Major bleeding	7 (4.0)	12 (6.8)	8 (7.3)	14 (12.6)	6 (3.0)	8 (3.9)	49 (3.1)	50 (3.5)
Recurrent ischaemia	21 (12.0)	33 (18.6)	13 (11.9)	14 (12.6)	27 (13.3)	39 (18.8)	16 (1.0)	47 (3.3)
Repeat intervention	6 (3.4)	10 (5.6)	12 (11.0)	6 (5.4)	15 (7.4)	22 (10.6)	139 (8.7)	122 (8.5)
Stroke	ND		0 (0)	2 (1.8)	1 (0.5)	3 (1.4)	21 (1.3)	20 (1.4)
Death, MI, or stroke	ND		11 (10.1)	12 (10.8)	25 (12.3)	33 (15.9)	153 (9.6)	162 (11.3)
Hospital stay (hrs), median (IQR)	55 (30–98)	77 (49–145)	96 (48–192)	120 (72–312)	120 (72–168)	168 (144–264)	ND	

MI, myocardial infarction; ND, no data; hrs, hours; IQR, interquartile range.
Values are presented as No. (%), unless otherwise indicated.

Katritsis DG, Siontis GCM, Kastrati A, et al. Optimal timing of coronary angiography and potential intervention in non-ST-elevation acute coronary syndromes. *Eur Heart J*. 2011;32(1):32-40.

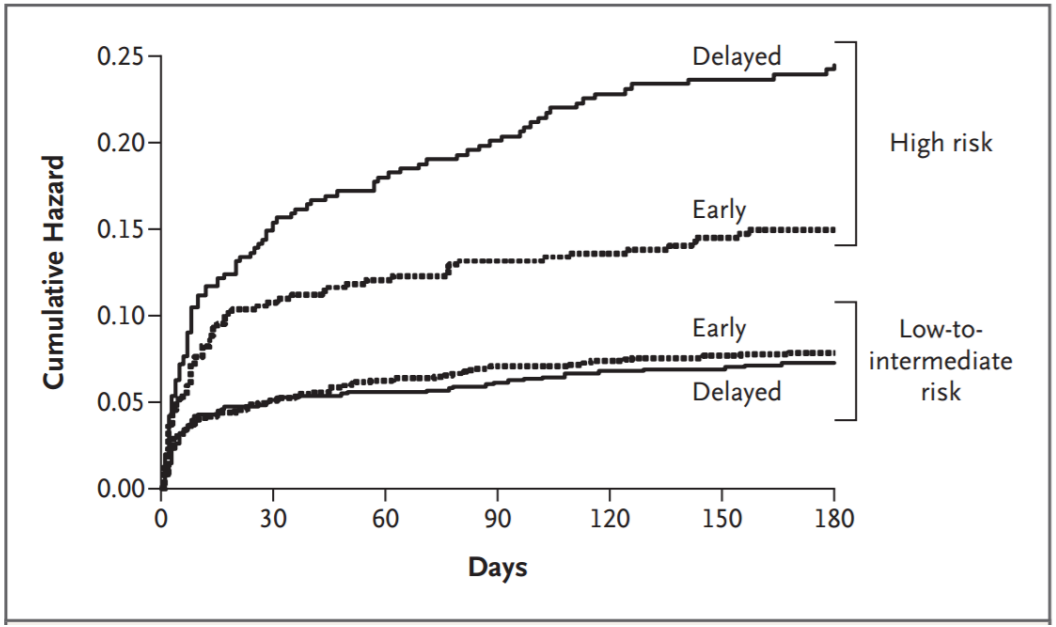


	E−D: difference (95% CI)
Hospital stay	2808 (4629-987)
Drugs	215 (690-260)
Procedures	28 (550-606)
Diagnostics	77 (176-22)
PCI	135 (380-650)
Total	2938 (5236-640)

Lamy A, Tong WR, Bainey K, Gafni A, Rao-Melacini P, Mehta SR. Cost Implication of an Early Invasive Strategy on Weekdays and Weekends in Patients With Acute Coronary Syndromes. *Can J Cardiol*. 2015;31(3):314-319.

Ischemia & CV outcomes

TIMACS



Grace >140

Grace ≤140

Mehta SR, Granger CB, Boden WE, et al. Early versus Delayed Invasive Intervention in Acute Coronary Syndromes. *N Engl J Med*. 2009;360(21):2165-2175.

TIMACS

Secondary outcome

Secondary outcome

Table 2. Primary and Secondary Outcomes.*

Variable	Early Intervention (N=1593)	Delayed Intervention (N=1438)	Hazard Ratio (95% CI)	P Value
	percent			
At 6 mo				
Death, myocardial infarction, or stroke	9.6	11.3	0.85 (0.68–1.06)	0.15
Death, myocardial infarction, or refractory ischemia	9.5	12.9	0.72 (0.58–0.89)	0.003
Death, myocardial infarction, stroke, refractory ischemia, or repeat intervention	16.6	19.5	0.84 (0.71–0.99)	0.04
Death	4.8	5.9	0.81 (0.60–1.11)	0.19
Myocardial infarction	4.8	5.7	0.83 (0.61–1.14)	0.25
Stroke	1.3	1.4	0.90 (0.49–1.68)	0.74
Refractory ischemia	1.0	3.3	0.30 (0.17–0.54)	<0.001
Repeat intervention	8.7	8.5	1.04 (0.82–1.34)	0.73
At 30 days				
Death, myocardial infarction, or stroke	6.7	7.6	0.88 (0.67–1.15)	0.34
Death, myocardial infarction, or refractory ischemia	6.6	9.3	0.70 (0.54–0.90)	0.006
Death, myocardial infarction, stroke, refractory ischemia, or repeat intervention	12.0	13.0	0.91 (0.75–1.12)	0.37
Death	2.9	3.3	0.86 (0.58–1.29)	0.48
Myocardial infarction	3.6	4.1	0.87 (0.61–1.25)	0.46
Stroke	0.9	0.9	1.04 (0.50–2.19)	0.91
Refractory ischemia	1.0	3.1	0.30 (0.17–0.55)	<0.001
Repeat intervention	5.9	4.2	1.39 (1.01–1.93)	0.05

Mehta SR, Granger CB, Boden WE, et al. Early versus Delayed Invasive Intervention in Acute Coronary Syndromes. *N Engl J Med*. 2009;360(21):2165-2175.

European Heart Journal (2011) 32, 32–40
doi:10.1093/eurheartj/ehq276

CLINICAL RESEARCH
Coronary heart disease

Optimal timing of coronary angiography and potential intervention in non-ST-elevation acute coronary syndromes

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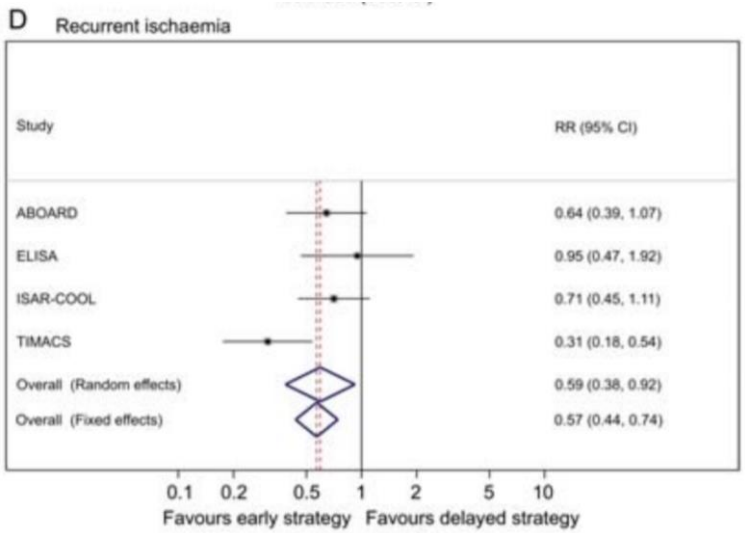
An invasive approach is superior to medical management for the treatment of patients with acute coronary syndromes without ST-segment elevation (NSTE-ACS), but the optimal timing of coronary angiography and subsequent intervention, if indicated, has not been settled.

We conducted a meta-analysis of randomized trials addressing the optimal timing (early vs. delayed) of coronary angiography in NSTE-ACS. Four trials with 4013 patients were eligible (ABOARD, ELISA, ISAR-COOL, TIMACS), and data for longer follow-up periods than those published became available for this meta-analysis by the ELISA and ISAR-COOL investigators. The median time from admission or randomization to coronary angiography ranged from 1.16 to 14 h in the early and 20.8–86 h in the delayed strategy group. No statistically significant difference of risk of death [random effects risk ratio (RR) 0.85, 95% confidence interval (CI) 0.64–1.11] or myocardial infarction (MI) (RR 0.94, 95% CI 0.61–1.45) was detected between the two strategies. Early intervention significantly reduced the risk for recurrent ischaemia (RR 0.59, 95% CI 0.38–0.92, $P = 0.02$) and the duration of hospital stay (by 28%, 95% CI 22–35%, $P < 0.001$). Furthermore, decreased major bleeding events (RR 0.78, 95% CI 0.57–1.07, $P = 0.13$), and less major events (death, MI, or stroke) (RR 0.91, 95% CI 0.82–1.01, $P = 0.09$) were observed with the early strategy but these differences were not nominally significant.

Early coronary angiography and potential intervention reduces the risk of recurrent ischaemia, and shortens hospital stay in patients with NSTE-ACS.

NSTE-ACS • Angiography • Timing • Meta-analysis



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JACC: CARDIOVASCULAR INTERVENTIONS
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Immediate Versus Delayed Invasive Intervention for Non-STEMI Patients

The RIDDLE-NSTEMI Study

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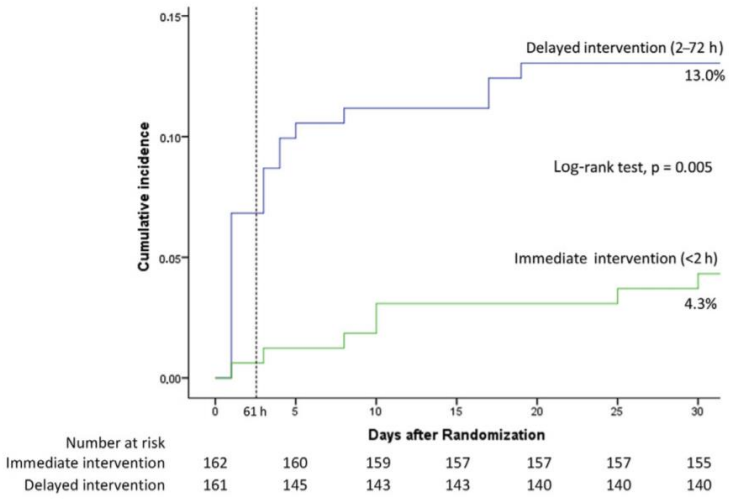
1 yr				
Death or MI	6.8	18.8	0.34 (0.17-0.67)	0.002
Death, MI, or recurrent ischemia	15.4	33.1	0.28 (0.15-0.51)‡	<0.001
Death§	4.9	5.6	0.87 (0.34-2.26)	0.78
MI	3.1	13.8	0.21 (0.08-0.55)	0.002
Recurrent ischemia	9.9	16.9	0.28 (0.12-0.63)‡	0.002
Major bleeding	0.6	3.1	0.20 (0.02-1.68)	0.14

FIGURE 2 Cumulative Incidence of the Primary Endpoint



Cumulative incidence of the combined primary endpoint of death or myocardial infarction at 30 days for immediate **(green line)** compared with delayed intervention **(blue line)**. **Dashed black line** intersecting the x-axis denotes the median time to angiography (61 h) in patients undergoing delayed invasive intervention.

Milosevic A, Vasiljevic-Pokrajcic Z, Milasinovic D, et al. Immediate Versus Delayed Invasive Intervention for Non-STEMI Patients: The RIDDLE-NSTEMI Study. *JACC Cardiovasc Interv*. 2016;9(6):541-549.

There is a tendency that earlier is better.

Early invasive therapy is safe.

Early invasive therapy reduces costs.

Early invasive therapy reduces ischemia and other CV outcomes.

Fernando Bátiz
fernando_batiz@me.com

There are specific scenarios for each strategy.

Patients should be assessed individually to select the best strategy for them.

Fernando Bátiz
fernando_batiz@me.com

Thank you!