THE VERDICT TRIAL

Very EaRly vs Deferred Invasive evaluation using Computerized Tomography

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on behalf of the **VERDICT** investigators

Disclosures

- Speakers fee Abbott
- Speakers fee Boston Scientific
- Advisory Board Novo Nordisk
- Advisory Board Bayer AS
- Advisory Board Asta Zeneca

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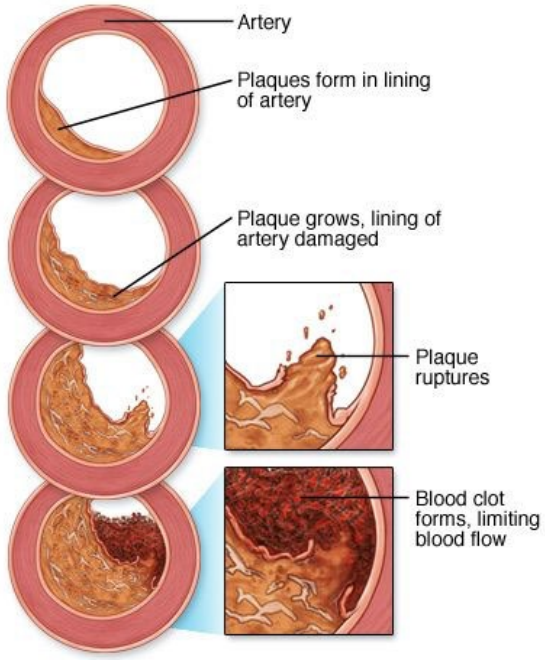
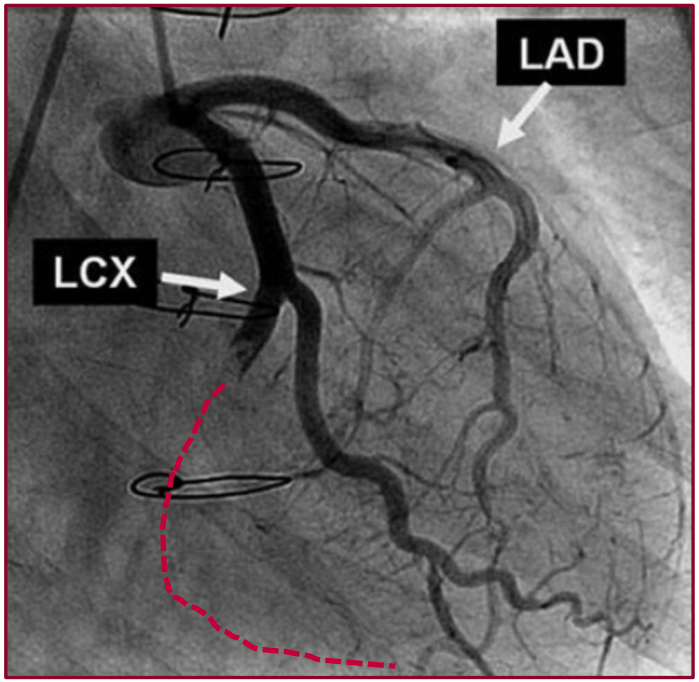
Background

Imminent vessel closure



ECG silent acute coronary occlusion



Guidelines

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 m^2)
• 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

Recommendations	Class[a]	Level[b]	Ref.[c]
An immediate invasive strategy (<2 h) is recommended in patients with at least one of the following 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 with refractory angina or ST deviation – recurrent dynamic ST- or T-wave changes, particularly with intermittent ST-elevation.	I	C	
An early invasive strategy (<24 h) is recommended in patients with at least one of the following high-risk criteria: – rise or fall in cardiac troponin compatible with MI – dynamic ST- or T-wave changes (symptomatic or silent) – GRACE score >140.	I	A	303, 326, 327

Pivotal VERDICT questions asked

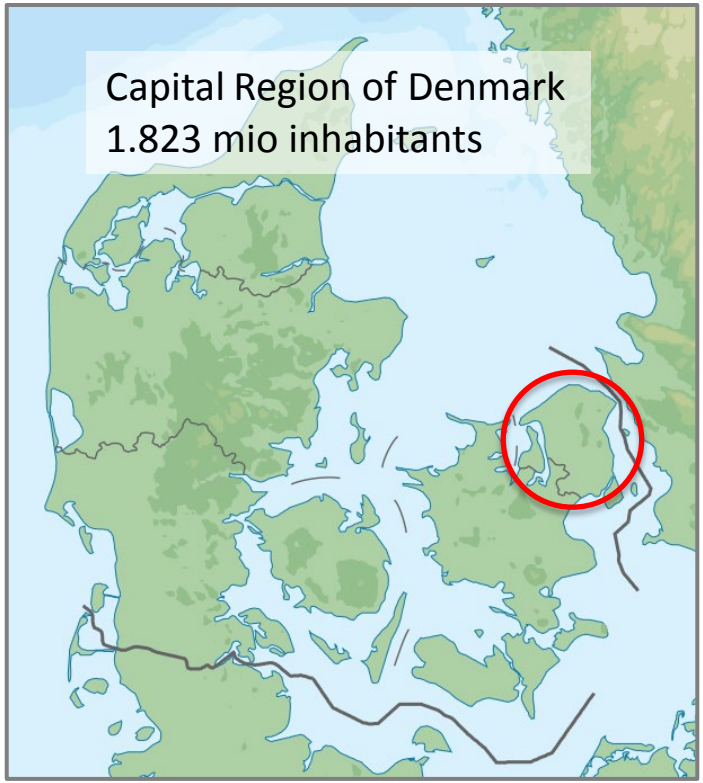
Would a very early (<12 hours) invasive strategy be favorable?

Would any effect of a very early invasive strategy last long term?

Principal hypothesis

Very early invasive investigation and possible revascularization within 12 hours is superior to a standard invasive investigation within 48-72 hours in patients admitted with non ST-segment elevation acute coronary syndrome

Randomized multicenter trial



Hillerød Hospital

Herlev Hospital

Glostrup Hospital

Hvidovre Hospital

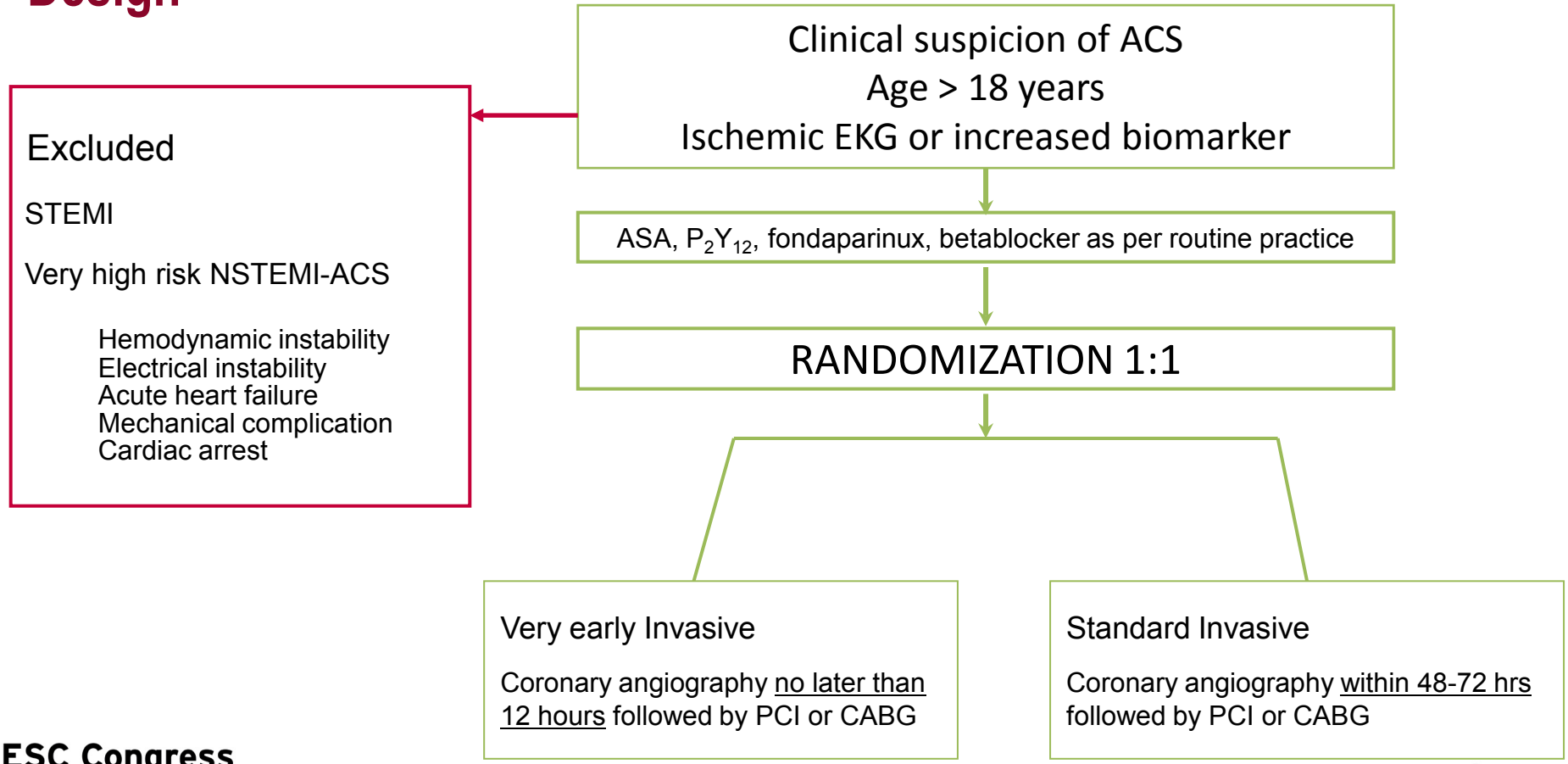
Bispebjerg/
Frederiksberg Hospital

Amager Hospital

Rigshospitalet

Gentofte Hospital

Design


Clinical suspicion of ACS
Age > 18 years
Ischemic EKG or increased biomarker
Excluded
STEMI
Very high risk NSTEMI-ACS
Hemodynamic instability
Electrical instability
Acute heart failure
Mechanical complication
Cardiac arrest
ASA, P_2Y_{12}, fondaparinux, betablocker as per routine practice
RANDOMIZATION 1:1
Very early Invasive
Coronary angiography no later than 12 hours followed by PCI or CABG
Standard Invasive
Coronary angiography within 48-72 hrs followed by PCI or CABG

Patient management

PCI was first choice revascularization strategy

Patients not feasible for PCI were allowed CABG

Full revascularization in MVD was encouraged but not mandatory if technically unfeasible

Primary endpoint

Composite

- All-cause death
- Non fatal recurrent myocardial infarction
- Hospitalization for heart failure
- Hospitalization for refractory myocardial ischemia

Power calculation

The trial was event driven

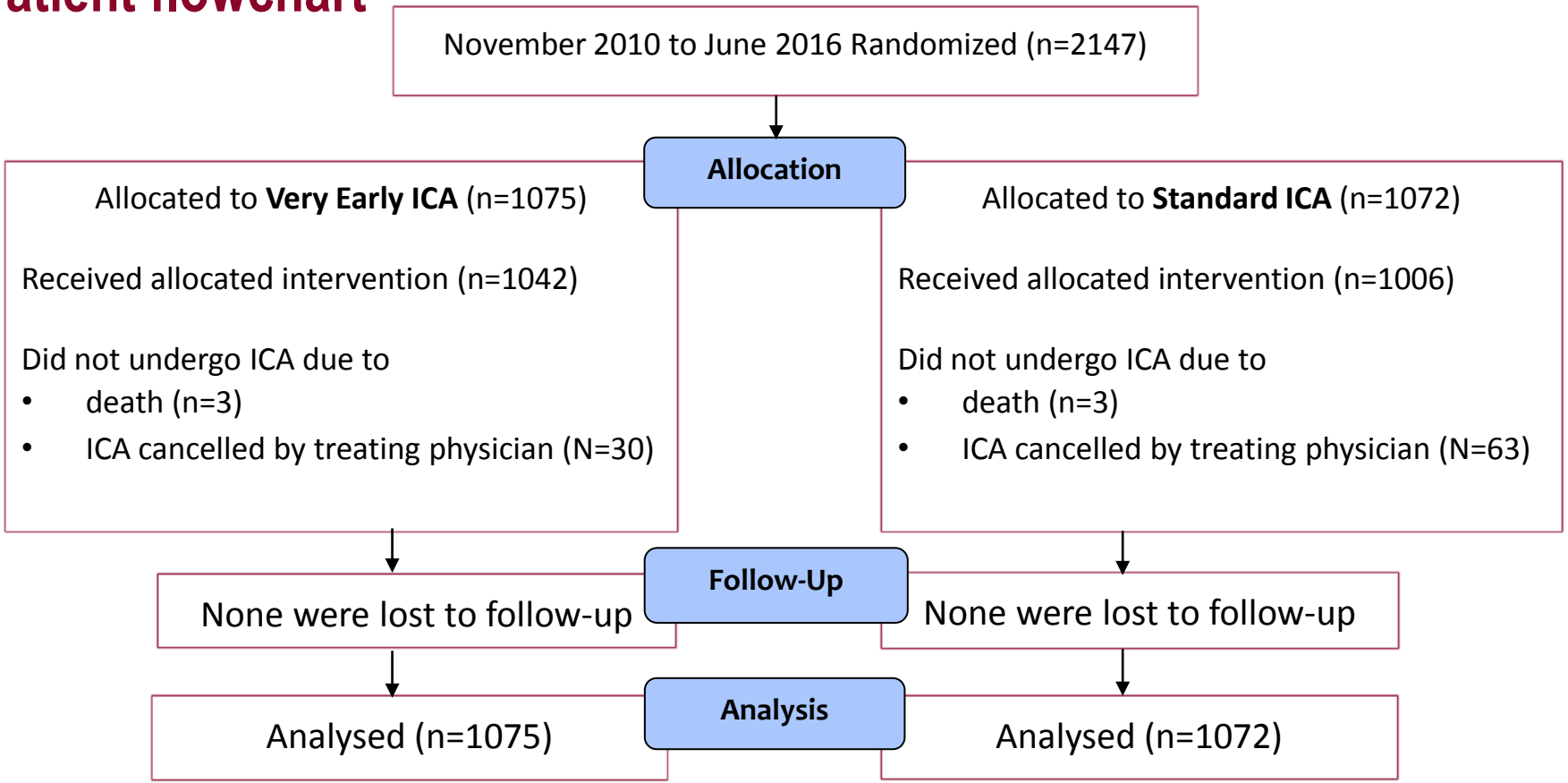
The expected event rate of the primary combined endpoint was 15% within 1 year and 50% within 4 years

A relative risk reduction of 25% with a power of 80% could be demonstrated with 711 patients in each group in order to obtain at least 375 primary events.

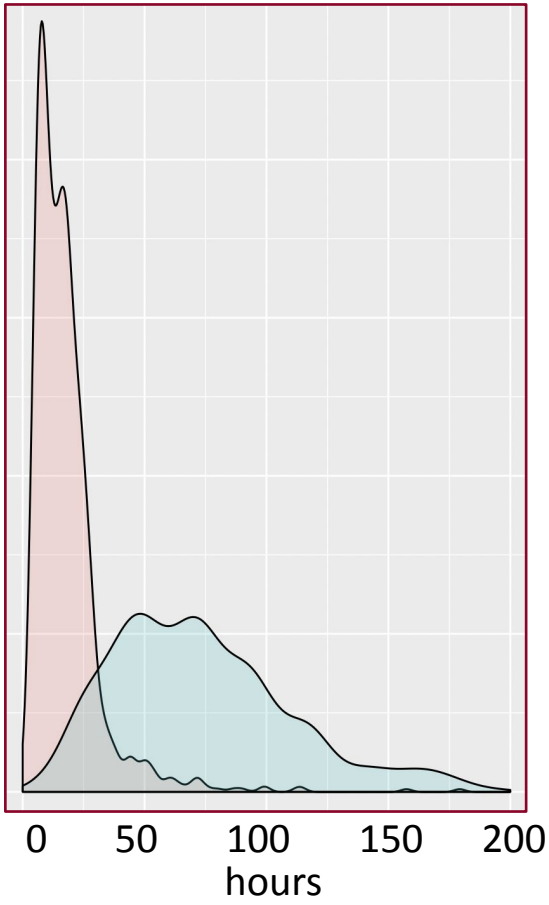
In order to potentially be able to demonstrate a reduction in mortality/heart failure hospitalization we aimed for a maximum of 2500 patients

Inclusion was stopped in June 2016 after inclusion of 2100 patients since it was stipulated that we would have more than 400 hard endpoints after additional 18 months of follow-up

Patient flowchart



Time to angiography



Very early = median 4.6 hours

Standard = median 61.6 hours

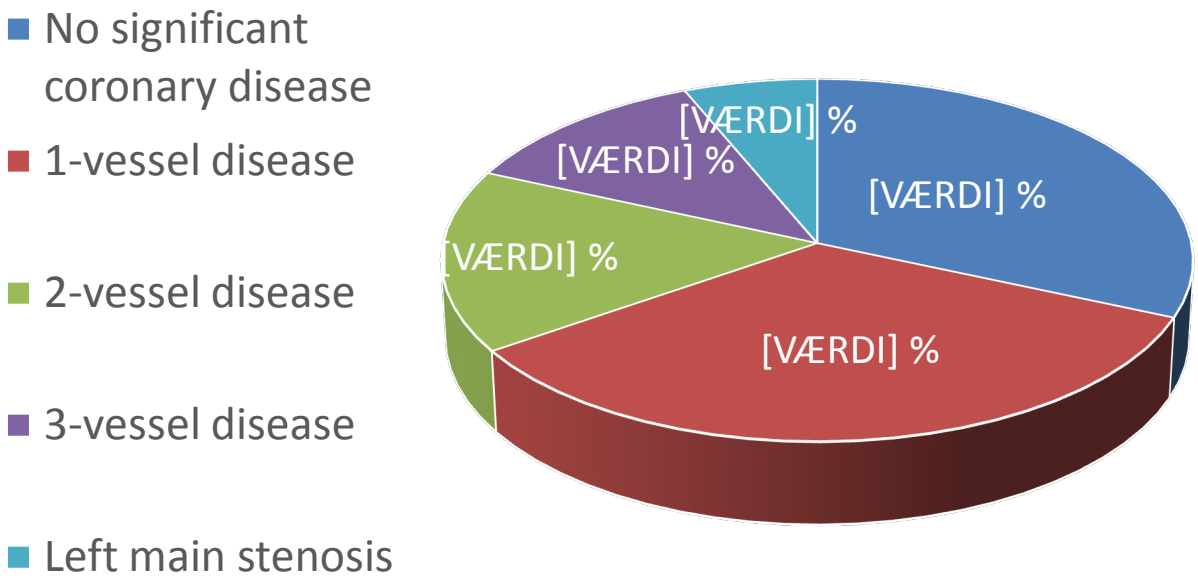
Baseline characteristics (I)

	Very Early (n=1075)	Standard (n=1072)	P-value
Male gender, n (%)	716 (66.6)	696 (64.9)	NS
Age in years, mean (SD)	63.6 (12.1)	63.6 (12.5)	NS
Prior smoker, n (%)	403 (37.5)	407 (38.0)	NS
Current smoker, n (%)	342 (31.8)	323 (30.1)	NS
Diabetes, n (%)	158 (14.7)	173 (16.1)	NS
Hypertension, n (%)	543 (50.5)	578 (53.9)	NS
Obstructive lung disease, n (%)	175 (16.3)	164 (15.3)	NS
Renal disease, n (%)	95 (8.8)	103 (9.6)	NS

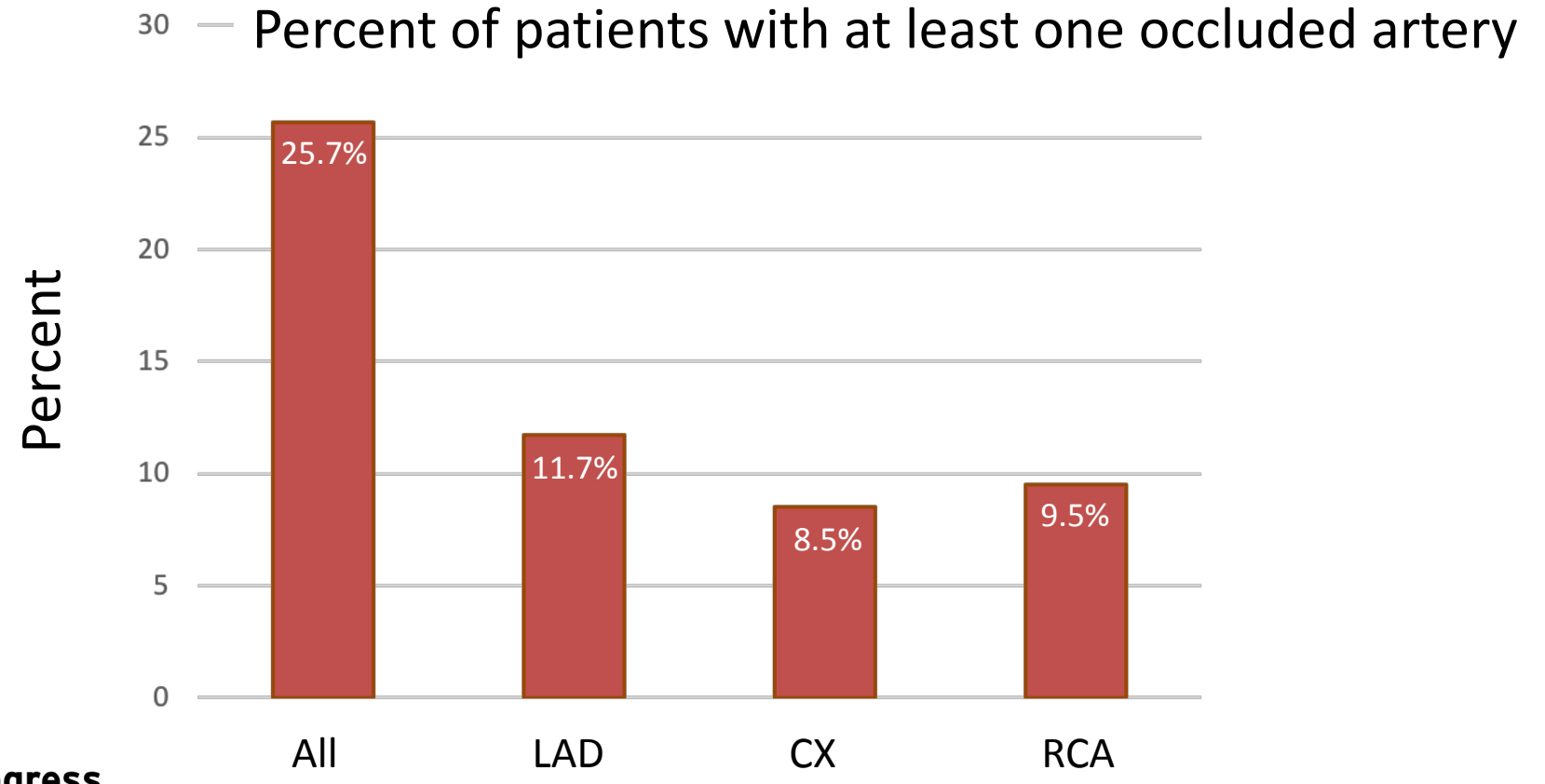
Baseline characteristics (II)

	Very Early (n=1075)	Standard (n=1072)	P-value
Previous stroke, n (%)	94 (8.7)	82 (7.6)	NS
History of CV disease	302 (28.1)	305 (28.5)	NS
Previous AMI, n (%)	186 (17.3)	186 (17.4)	NS
Previous PCI, n (%)	151 (14.0)	163 (15.2)	NS
Previous CABG, n (%)	57 (5.3)	57 (5.3)	NS
GRACE score, mean (SD)	141.3 (29.8)	140.8 (31.4)	NS
GRACE score >140, n (%)	520 (49.3)	505 (48.7)	NS
ECG with new ischaemia, n (%)	648 (61.1)	640 (60.8)	NS
Elevated Troponin, n (%)	871 (81.2)	847 (79.2)	NS

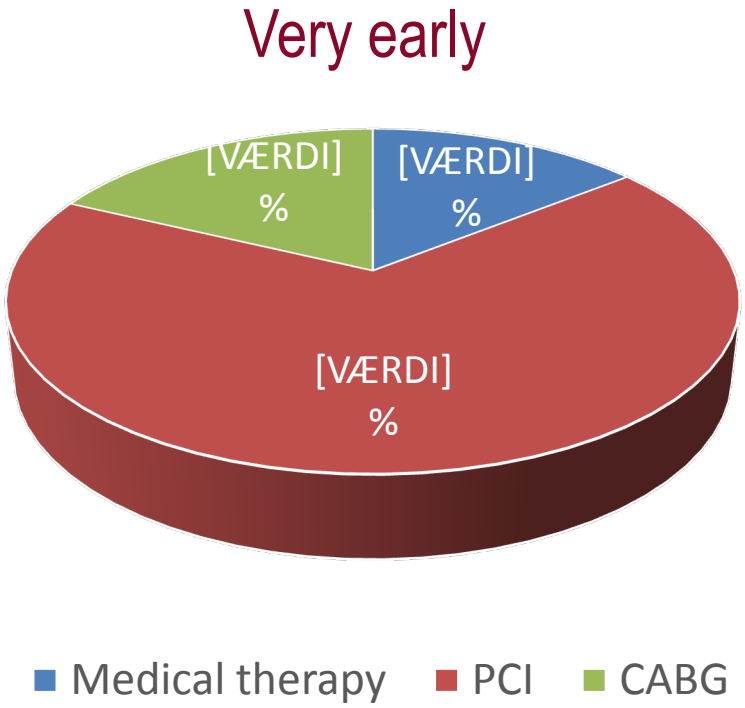
Coronary findings

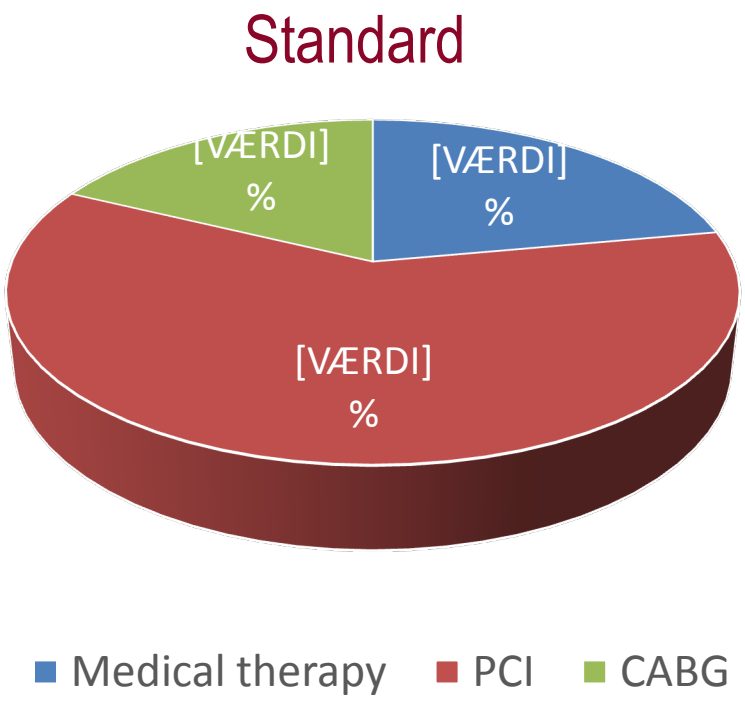


Coronary findings



Therapy of patients with significant coronary artery disease





Procedural characteristics

Number of treated lesions (p=0.65)

	Very Early (n=1075)	Standard (n=1072)
1	385 (77.3)	354 (80.1)
2	85 (17.1)	71 (16.1)
3	21 (4.2)	13 (2.9)
4	3 (0.6)	2 (0.5)
5	0	0
6	2 (0.4)	0 (0.0)

Number of stents used (p=0.48)

	Very Early (n=1075)	Standard (n=1072)
0	46 (9.2)	37 (8.4)
1	298 (59.8)	286 (64.7)
2	111 (22.3)	94 (21.3)
3	28 (5.6)	18 (4.1)
4	10 (2.0)	6 (1.4)
5>=	4 (0.8)	1 (0.2)

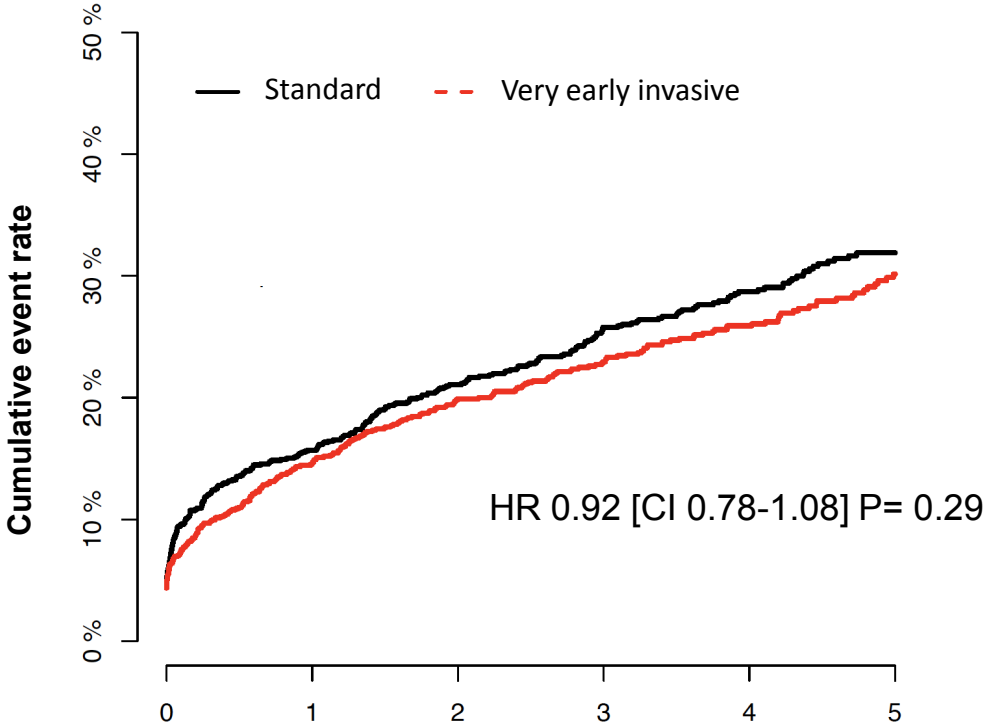
Procedural characteristics (II)

	Very Early (n=1075)	Standard (n=1072)	P-value
Drug eluting stent	425 (85.3)	383 (86.7)	NS
Staged PCI	8 (0.7)	8 (0.7)	NS
Complete revascularization by PCI, n (%)	379 (76.1)	347 (78.5)	0.05
Median procedural time (IQR)	10.0 (7.0-18.0)	13.0 (9.0-20.0)	0.0005
Radiation (mSv), median (IQR)	2.3 (1.6-4.1)	2.7 (1.8-5.4)	0.008
Periprocedural complications			
Cardiac arrest	3 (0.3)	4 (0.4)	NS
Bleeding	19 (1.8)	19 (1.8)	NS
Stroke/TIA	6 (0.6)	4 (0.4)	NS
AMI	1 (0.1)	5 (0.5)	NS

Medication at discharge

	Very Early (n=1075)	Standard (n=1072)	P-value
Aspirin, n (%)	878 (81.7)	891(83.1)	NS
Ticagrelor, n (%)	500 (46.5)	500 (46.6)	NS
Clopidogrel n (%)	228 (21.2)	236 (22.0)	NS
Prasugrel n (%)	22 (2.0)	17 (1.6)	NS
Warfarin/NOAC n (%)	78 (7.2)	70 (6.5)	NS

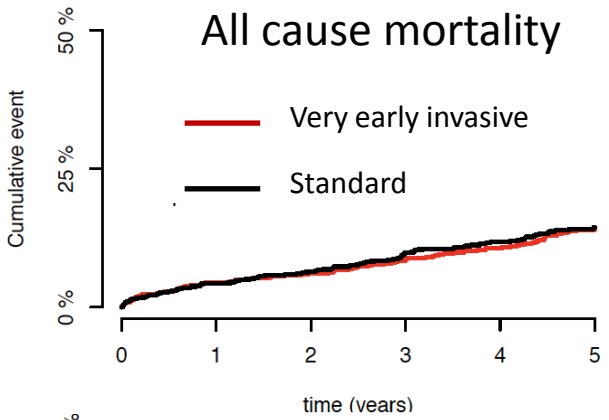
Primary endpoint – median follow up 4.3 years

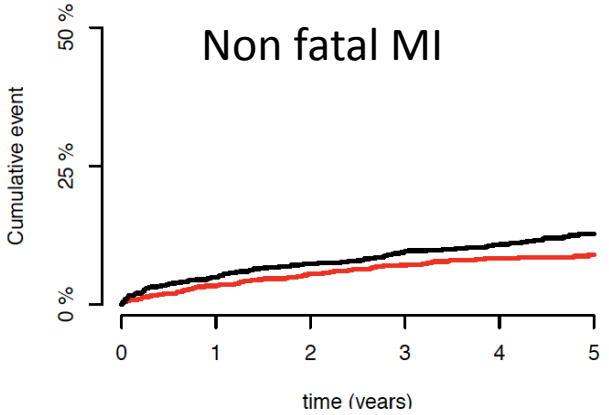


No. at Risk						
Standard	1072	898	799	627	440	241
Very early	1075	914	814	640	456	252

Secondary endpoints

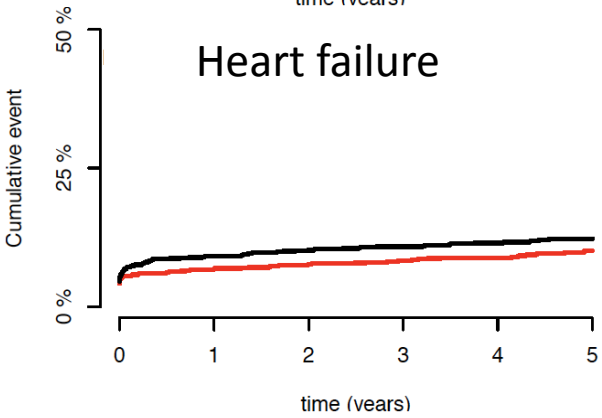
HR 0.97
[CI 0.76-1.23]
P= 0.79

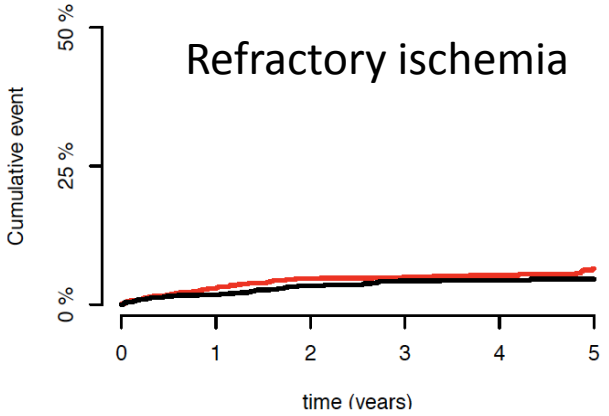




HR 0.73
[CI 0.56-0.96]
P= 0.025

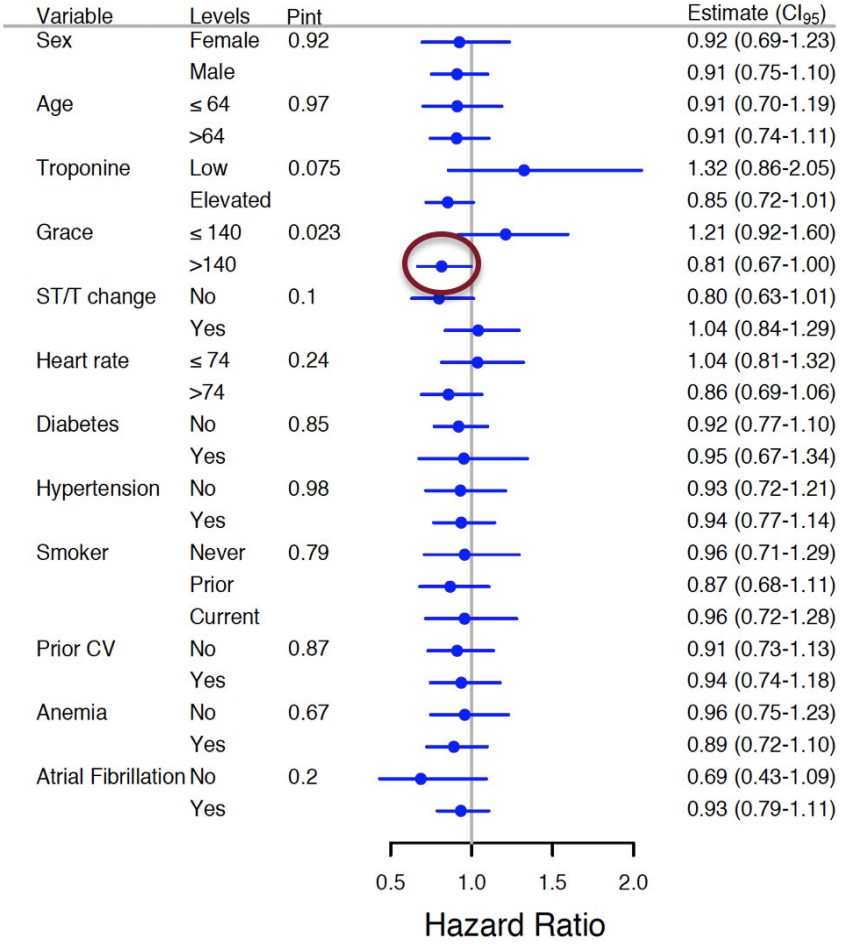
HR 0.78
[CI 0.60-1.01]
P= 0.06



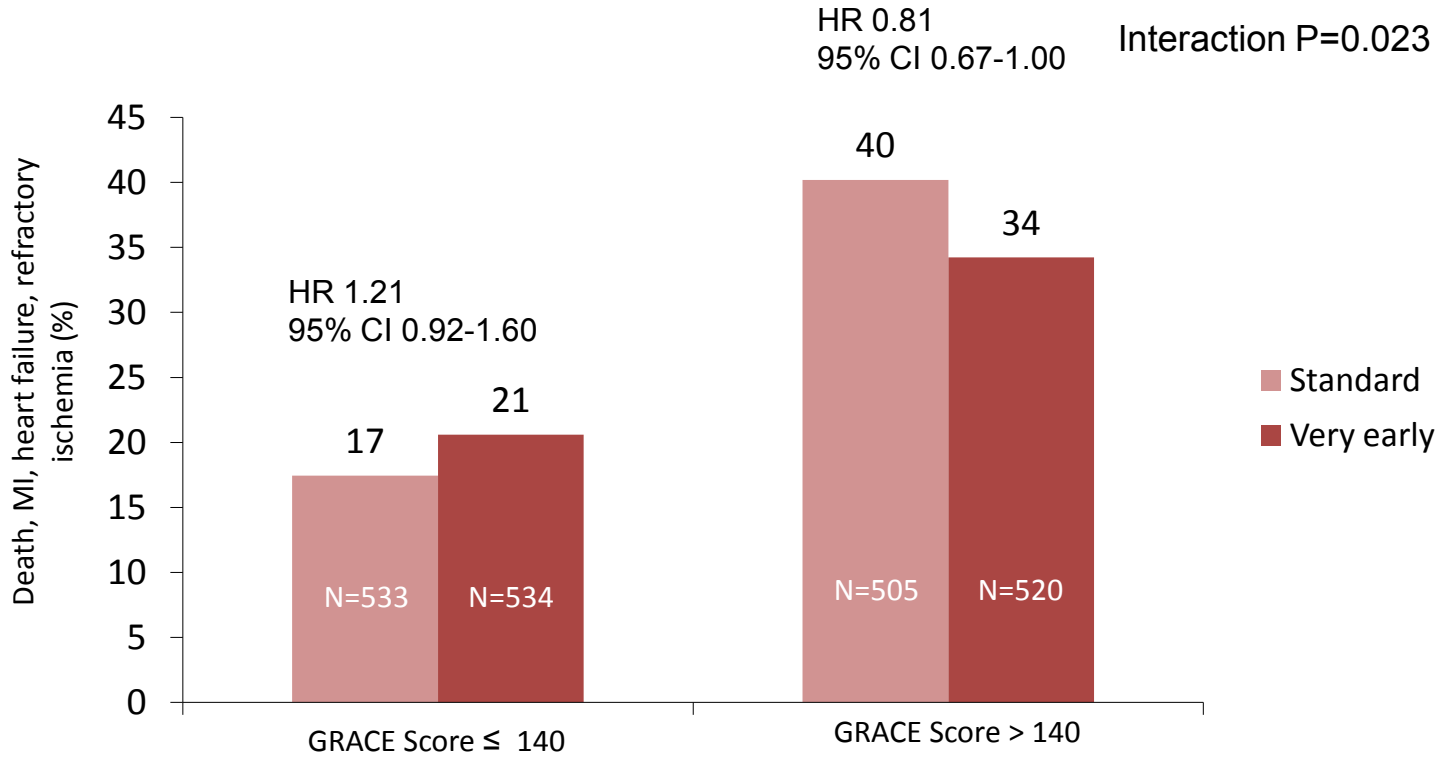


HR 1.32
[CI 0.91-1.91]
P= 0.14

Subgroup analysis



GRACE Risk Score: Primary Endpoint



Conclusion

A strategy of very early invasive investigation in patients with NSTEMI ACS does not improve a long-term composite outcome of all-cause death, non fatal recurrent myocardial infarction, hospitalization for heart failure or hospitalization for refractory myocardial ischemia

However, a subgroup of patients with a GRACE score > 140 showed significantly improved outcome as compared to standard care

Implications

A very early invasive look-up in NSTEMI ACS is safe and possibly favorable for some

Given, however, the high number of NSTEMI patients (30% without coronary disease), acute investigation is logistically challenging and potentially not cost-effective

Nonetheless, patients that present with symptoms of ACS, have troponin rise and a high GRACE should be examined within 12 hours

VERDICT investigators

Circulation

10.1161/CIRCULATIONAHA.118.037152

Early versus standard care invasive examination and treatment of patients with Non-ST-segment elevation acute coronary syndrome

The VERDICT (Very EaRly vs Deferred Invasive evaluation using Computerized Tomography) – randomized controlled trial

Short title: *Early invasive strategy in acute coronary syndrome*

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