

Immediate angioplasty compared to ischemia-guided management after thrombolysis for ST-elevation myocardial infarction in areas with very long transfers.

**Results of the NORwegian study on
District treatment of
ST-Elevation Myocardial Infarction
NORDISTEMI**

Sigrun Halvorsen, MD, PhD

Ellen Bøhmer MD, Harald Arnesen MD, PhD

Oslo University Hospital, Ullevål, Oslo, Norway

Disclosure

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Background

- Primary PCI is the preferred treatment of ST-elevation myocardial infarction
- However, in many areas of the world, primary PCI cannot be performed within the recommended time limits (<90-120 min)
- In these remote areas, thrombolysis is still the treatment of choice
- Optimal treatment after thrombolysis for STEMI in rural areas remains unclear



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Objective

- To compare 2 different strategies after thrombolysis for ST-elevation myocardial infarction, **in patients with very long transfer times (> 90 min):**
 - A. Immediate transfer for angiography/PCI
 - B. Conservative, ischemia-guided treatment

Inclusion criteria

1. Age 18 -75 years
2. Symptoms of MI for < 6 hours
3. ST-segment elevation ≥ 1 mm in two contiguous extremity leads or ≥ 2 mm in two contiguous precordial leads or new LBBB
4. Expected time delay from first medical contact to PCI >90 minutes
5. Receiving thrombolytic treatment with tenecteplase (TNK)
6. Informed consent for participation

Exclusion criteria

1. Any standard contra-indication for thrombolytic treatment
2. Known serious renal failure (creatinine >250 mmol/l)
3. Cardiogenic shock at randomization
4. Diseases with life expectancy < 12 months
5. Pregnancy
6. Alcoholism, drug abuse, mental retardation, dementia, psychiatric disease or other conditions that severely reduce compliance

Study region

South-Eastern part
of Norway



400 km

X PCI centre



NORDISTEMI Study design

Acute STEMI < 6 hours
Expected time delay to PCI > 90 min
≤ 75 years

Aspirin 300 mg, Tenecteplase (TNK)
Enoxaparin 30 mg iv + 1mg/kg sc, Clopidogrel 300mg

1:1

A

**Immediate transfer for
angiography/PCI**

B

**Ischemia-guided treatment in
local hospitals with transfer for
rescue PCI if needed**

**Clinical follow-up: 1, 3, 7, 12 months
SPECT: 3 months**

Outcome

- **Primary endpoint:**
 - A composite of death, reinfarction, stroke or new ischemia within 12 months
- **Secondary endpoints:**
 - A composite of death, reinfarction or stroke within 12 months
 - Bleeding complications within 30 days
 - Transport complications
 - Infarct size at 3 months (SPECT)
 - Quality of life during 12 months
 - Total costs over 12 months

Power calculation

- Based on previous results*, the occurrence of the primary endpoint at 12 months was expected to be 30% in the conservative group and 15% in the early invasive group (50% reduction)
- With a two-sided alpha of 5% and a power of 80%, 133 patients in each group were required

*SIAM III. J Am Coll Cardiol 2003; 42:634-41, GRACIA-1. Lancet 2004;364: 1045-53

NORDISTEMI flow chart

526 patients treated for STEMI with tenecteplase
were screened

266 patients were included

134 assigned
invasive strategy

132 assigned
conservative strategy

134 completed 12 months F-UP

132 completed 12 months F-UP

Baseline characteristics 1

	Invasive group n = 134	Conservative group n = 132	p
Age, years (SD)	60 (9.0)	60 (9.8)	0.98
Men	107 (80%)	94 (71%)	0.13
Treated hypertension	33 (25 %)	50 (38 %)	0.03
Smokers	106 (79 %)	104 (79 %)	0.93
Diabetes mellitus	8 (6 %)	10 (8 %)	0.78
Total cholesterol, mmol/l	5.2 (1.1)	5.4 (1.1)	0.11
Previous MI	15 (11 %)	14 (11 %)	0.97

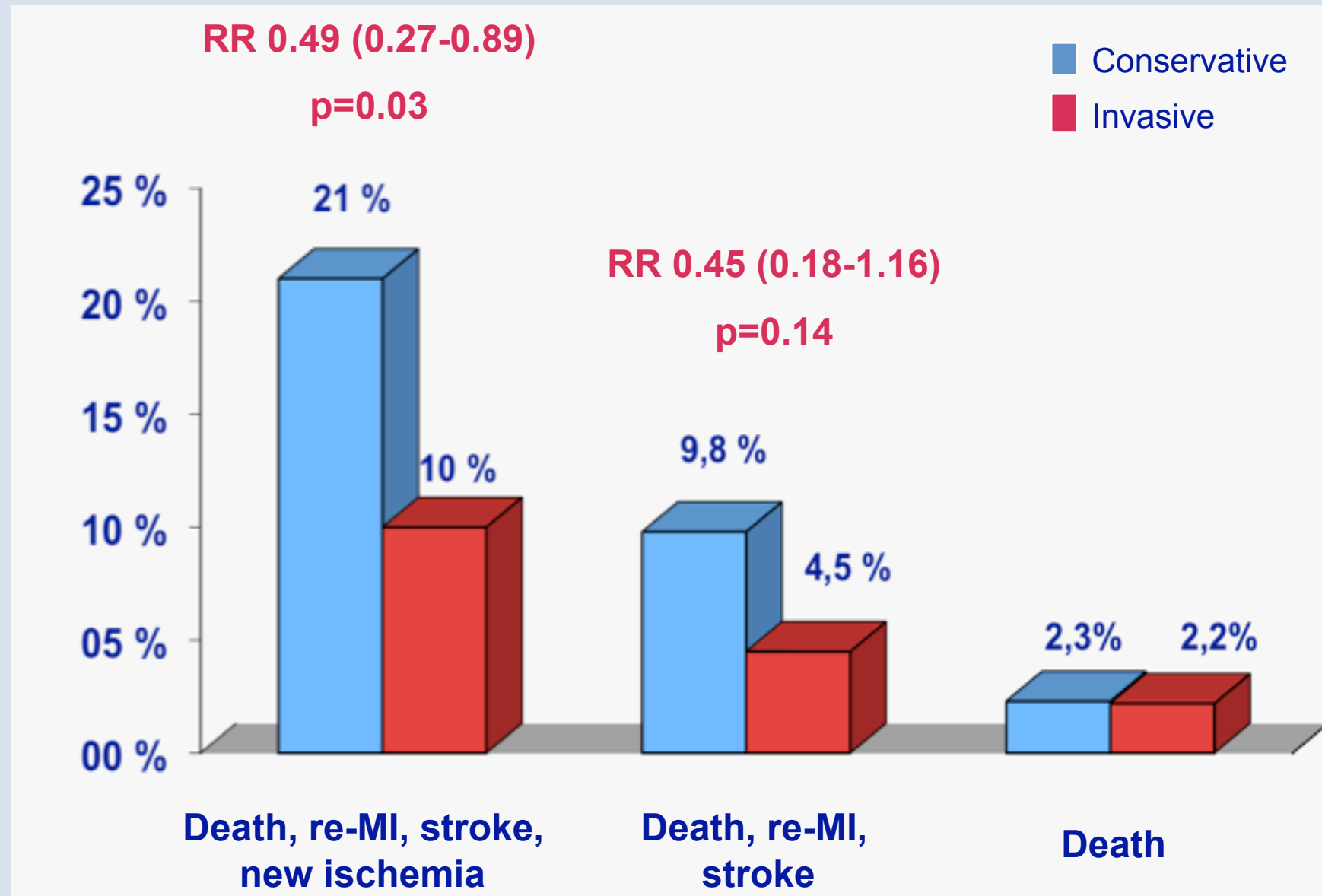
Baseline characteristics 2

	Invasive group n = 134	Conservative group n = 132	p
Mean BP before thrombolysis:			
Systolic BP (mmHg)	133.4 (22.9)	134.2 (22.4)	0.74
Diastolic BP (mmHg)	80.7 (15.2)	82.0 (15.9)	0.48
Anterior infarct location	59 (44%)	51 (39%)	0.44
Median time from symptom onset to thrombolysis (min)	117 (80, 195)	126 (80, 195)	0.72

Invasive procedures

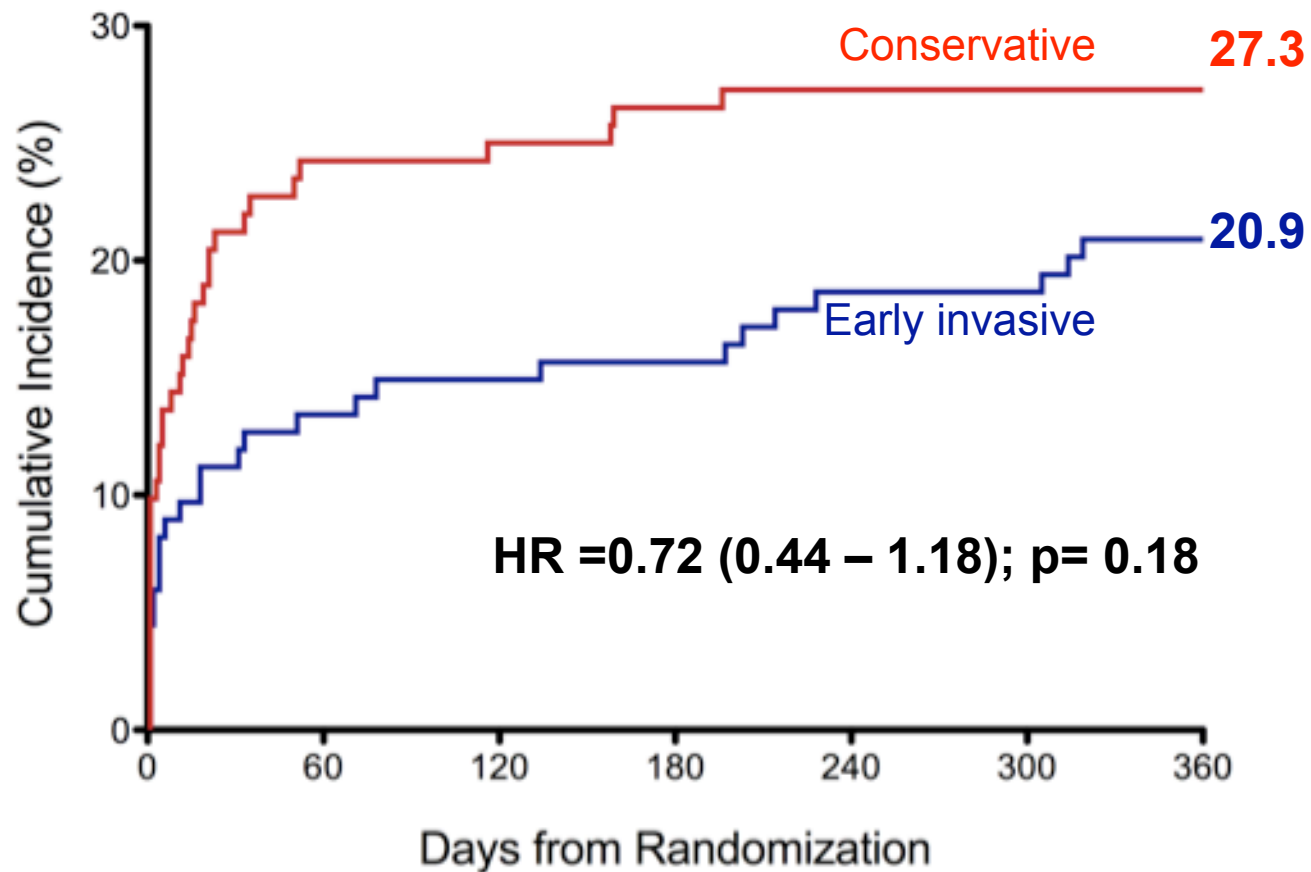
	Invasive group n=134	Conservative group n=132
Angiography performed	133 (99%)	125 (95%)
TNK to arrival at cathlab	130 (105, 155) min	5.5 (0, 17.5) days
PCI performed	119 (89%)	94 (71%)
TNK to first balloon	163 (137, 191) min	3.0 (0, 13) days
Median transfer distance to PCI	158 (129, 200) km	
Radial access	111 (83%)	118 (89%)
Stents implanted	115 (86%)	90 (68%)
Abciximab	16 (14%)	8 (6%)
CABG performed	9 (7%)	16 (12%)

Clinical outcome at 30 days



Kaplan-Meier curve for Primary Endpoint

12-month Death, Reinfarction, Stroke or new Ischemi

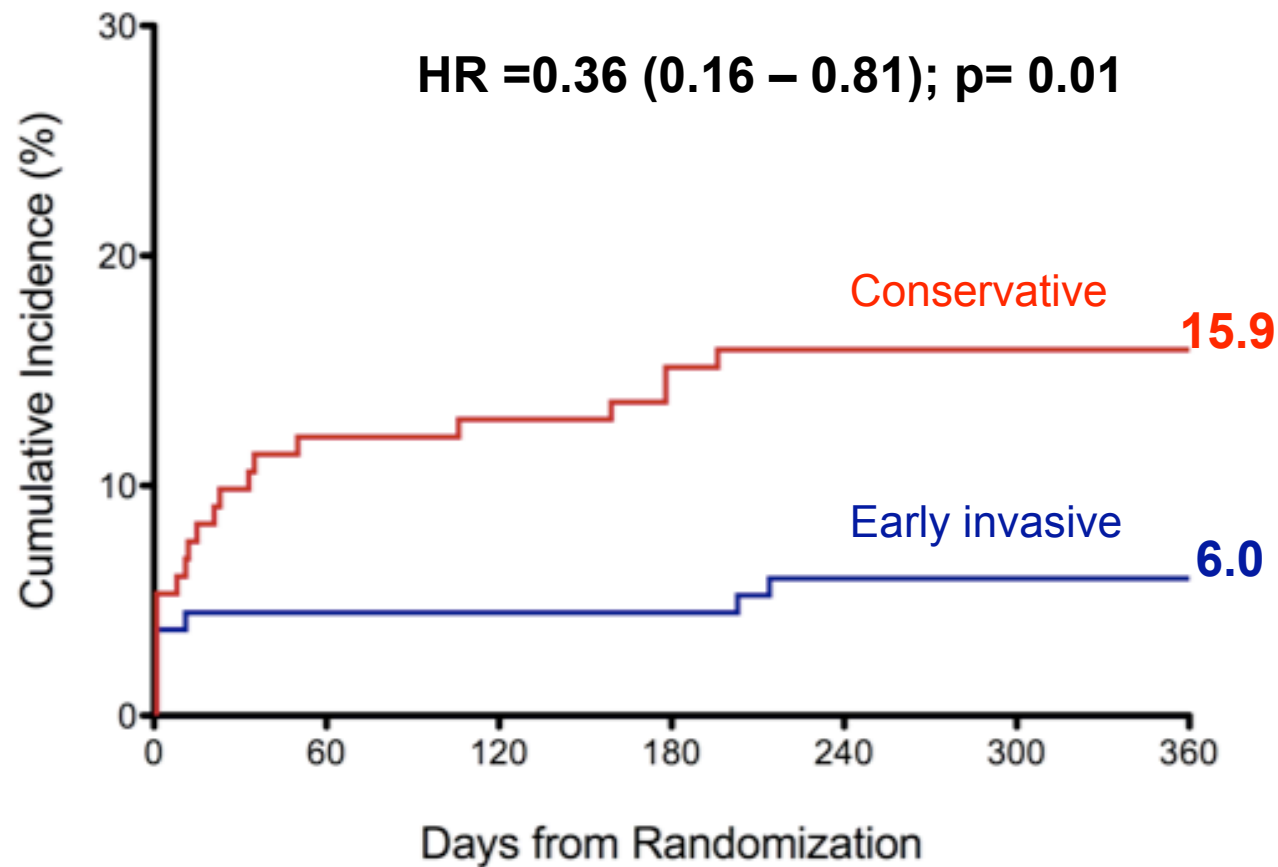


No. At Risk

Conservative group	132	100	99	97	96	96	96
Early invasive group	134	116	114	113	109	109	106

Kaplan-Meier curve for Secondary Endpoint

12-month Death, Reinfarction or Stroke



No. At Risk

Conservative group	132	116	115	114	111	111	111
Early invasive group	134	128	128	128	126	126	126

30-day bleeding events

GUSTO classification

	Invasive group n = 134	Conservative group n = 132	p
Severe	2 (1.5%)	3 (2.3%)	
Moderate	0 (0%)	3 (2.3%)	
Minor	14 (10%)	13 (9.8%)	
Total bleeding events	16 (13 %)	19 (14 %)	0.68

Transport Complications

Median transfer distance to PCI: 158 (129, 200) km

	Invasive group n = 134	Conservative group n = 132
Death	1 (0.7%)	0
Ventricular Fibrillation	4 (3.0%)	0
Ventricular Tachycardia	0	2 (1.5%)

Summary

- An early invasive strategy after thrombolysis reduced the primary endpoint including ischemia at 12 months compared to a conservative strategy, but the reduction did not reach statistical significance (HR 0.72, $p=0.18$)
- At 30 days, however, the reduction in the composite endpoint including ischemia was significant (21% vs 10%, $p=0.03$)
- The secondary endpoint (composite of death, reinfarction or stroke within 12 months) was significantly reduced in the early invasive group (HR 0.36, 95% CI 0.16-0.81, $p=0.01$)
- No difference between groups in bleeding complications
- Few transport complications

NORDISTEMI

Conclusion

- Although the reduction in the primary outcome, including the softer endpoint ischemia, did not reach statistical significance at 12 months, the significant reduction in the rate of death, reinfarction and stroke suggest that an early invasive strategy may be the preferred option following thrombolysis, also in areas with very long transfer times
- These findings might be taken into consideration when making algorithms for treatment of STEMI in rural areas

Contributors

- **NORDISTEMI Steering committee:** Sigrun Halvorsen (Chairman), Harald Arnesen, Pavel Hoffmann, Michael Abdelnoor, Arild Mangschau, Ivar S Kristensen (Oslo, Norway)
- **Clinical Events Committee:** Tor O Klemsdal, Kolbjørn Forfang (Oslo, Norway)
- **Community Hospitals:** Ellen Bohmer (Coordinator), M German, I Popovic, T Myhrvold, BU Engen, A Kravdal, T Grønvold, M Jørgensen, B Hansen, P Ofstad, Ø Rose, BT Sørli
- **PCI site:** S Halvorsen, E Bohmer, P Hoffmann, C Muller, R Bjørnerheim, G Smith, I Seljeflot, A Mangschau
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DIstrict treatment of ST-Elevation Myocardial Infarction)

Ellen Bøhmer, MD,* Pavel Hoffmann, MD, PHD,† Michael Abdelnoor, PHD,‡
Harald Arnesen, MD, PHD,§ Sigrun Halvorsen, MD, PHD||

Oslo and Lillehammer, Norway

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