What do to with late comer and/or non-reperfused STEMI patients

Lession from ISACS-TC

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International Survey of Acute Coronary Syndromes in Transitional Countries (ISACS-CT) Rationale and Design 1

- Mortality from cardiovascular disease has been decreasing continuously in the United States and many Western European countries, but it has increased or remained unchanged in many of the states of Eastern Europe. Analysis of this phenomenon has been hindered by insufficient information.

- Much has been hypothesised about the ethnicity- and poverty-associated disparities in mortality when comparing Eastern with Western European countries.

- Yet, identifying underlying causes for these worrisome geographic health patterns continues to challenge health care providers and researchers.

International Survey of Acute Coronary Syndromes in Transitional Countries (ISACS-CT) Rationale and Design 2

Both a retrospective (over a one year period) and prospective (over a three year period) study which was designed in order to obtain data of patients with acute coronary syndromes in countries with economy in transition, and herewith control and optimize internationally guideline recommended therapies in these countries.

There are a total of 132 Collaborating Centers in 17 transitional countries (Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Hungary, Kosovo, Moldova, Latvia, Lithuania, Poland, Russian Federation, Romania, Macedonia, Serbia, Slovakia, Slovenia, Ukraine) and a total of 40 centers in 2 industrialized countries (Italy, United Kingdom) that serve as control.

http://isacs-ct.cineca.org/

International Survey of Acute Coronary Syndromes in Transitional Countries (ISACS-CT) Rationale and Design 3

- Reporting the characteristics of all patients presenting to the enrolled centers with STEMI or NSTEMI/UA;
- Monitoring in-hospital outcome, and outcome rates at 6-month and 1 year;
- Exploring interventional cardiac procedures and related complications;
- Examining the therapeutic regimens and investigation conformity of treatment with already established guidelines.

http://isacs-ct.cineca.org/

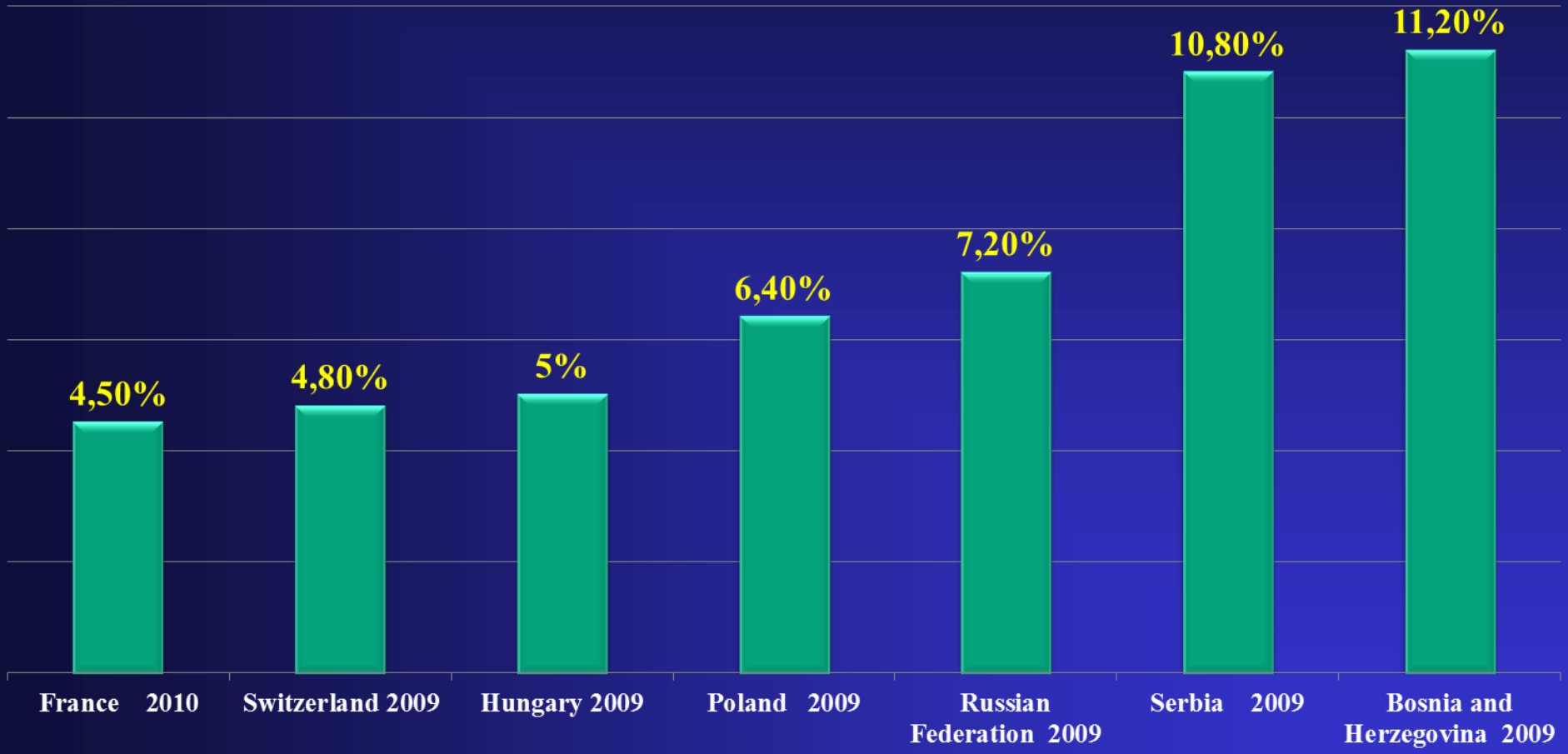
Reperfusion Therapy

	Hungary N=8800	Russian Federation N=5796	Serbia N=7555	Bosnia and Herzegovina N=1335	p-value
Time from symptom onset to admission (median)	210 min	133min	180 min	366 min	<0.001
Reperfusion therapy	72%	43.7%	52%	42.2%	
Fibrinolysis	2%	23.1% †	30%	23.9%	<0.001
primary PCI	70%	20.6%	22%	18.3%	
Not reperfused patients	28%	56.3%	48%	57.8%	<0.001
Patient admitted within 12 hours without reperfusion therapy	2%	27.9%	34%	10.8%	<0.001

†Fibrinolysis + 0.6 % Rescue PCI

Bugiardini et al. Current Vascular Pharmacology, 2013

In-hospital STEMI case fatality rates across the OECD countries for the period 2009-2010



*Data from ISAC-TC, FAST-MI 2010, AMIS Plus: Swiss registry and the Polish Registry of Acute Coronary Syndromes (PL−ACS)

Bugiardini et al. Current Vascular Pharmacology, 2013

CONCLUSION

•We found that the care of Russian Federation, Bosnia and Herzegovina and Serbian patients with STEMI was characterized by limited use of appropriate reperfusion therapy.

•Lack of reperfusion therapy translates into worse outcomes.

•Differences in time delay from symptoms onset to hospital admission may have strongly influenced STEMI patients' outcome.

Bugiardini et al. Current Vascular Pharmacology, 2013

Optimal Acute Therapeutic Strategies in STEMI not Receiving Reperfusion Therapy

Bugiardini R., Dorobantu M, Vasiljevic Z., Kedev S., Knežević B., Miličić D, Calmac L., Trninic D., Daullxhiu I., Cenko E, Martelli I., Manfrini O., Koller, A., Badimon L.;
on the Behalf of the ISACS-TC Investigators and the Working Group on Coronary Pathophysiology & Microcirculation of the European Society of Cardiology.

The demonstration of the benefit of early reperfusion with fibrinolytic agents was a major advance leading to a reduction in morbidity and mortality in patients with acute STEMI.

The development of primary PCI for acute myocardial infarction (MI) has extended the benefit of early reperfusion to include some patients ineligible for thrombolysis.

Despite the increasing use of primary PCI, the proportion of eligible patients undergoing early reperfusion with either fibrinolytic agents or primary PCI remained constant, at about 70%, from 1994 through 2006,with roughly 30% of patients receiving neither reperfusion therapy.

Missed Opportunities for Reperfusion

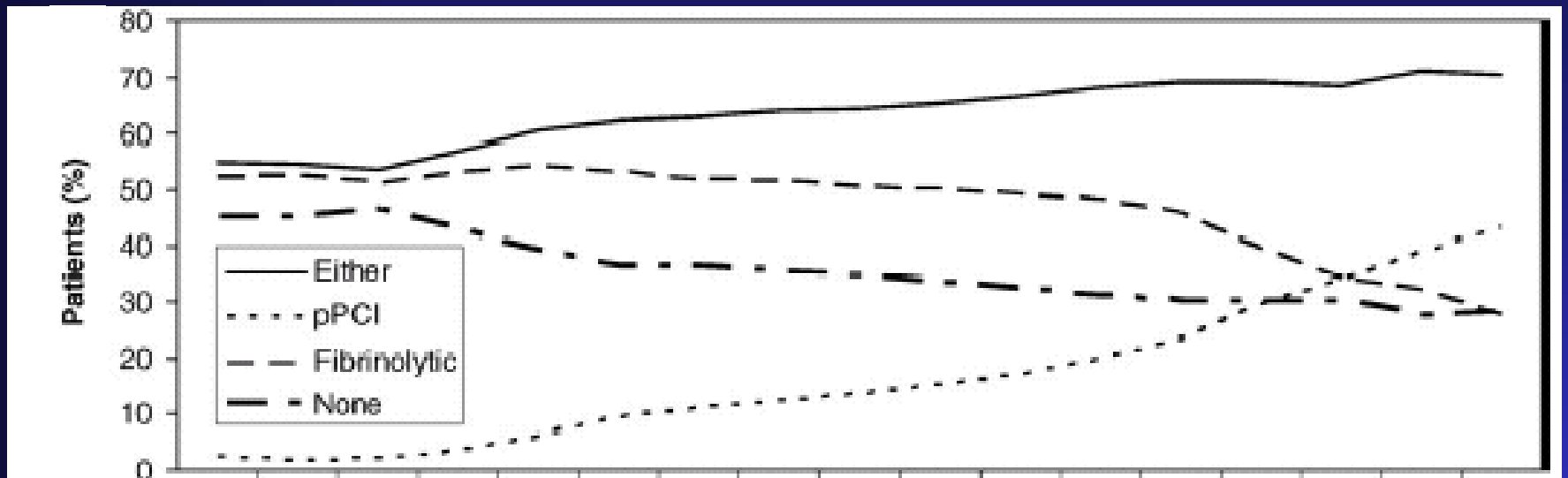
ST ↑ or LBBB, <12 hrs from onset, no contraindications

	ANC (%)	US (%)	AB (%)	EUR (%)
n	269	327	339	739
PCI alone	1.1	17.7	13.9	16.2
Lytic alone	66.9	30.6	53.1	49.4
Both	2.2	18.7	5.0	4.9
Neither	**29.7**	**33.0**	**28.0**	**29.5**

ANC, Australia/New Zealand/Canada; US, United States; AB, Argentina/Brazil; EUR, Europe

Eagle KA et al. Lancet 2002;359:373-7.

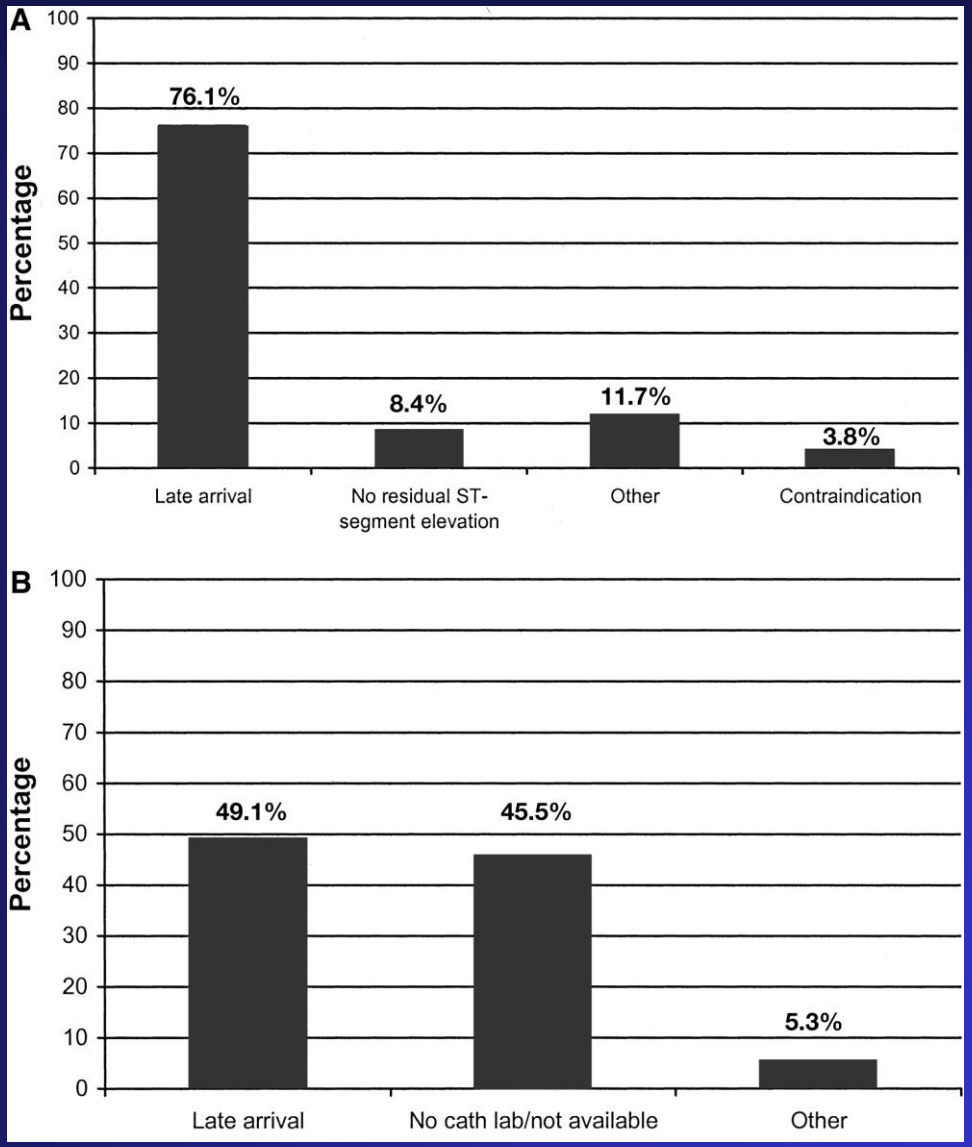
Trends in reperfusion strategies among The National Registry of Myocardial Infarction



	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
Either	55.1	54.8	53.7	57.1	60.7	62.5	62.9	64	64.3	65.5	66.6	68.2	69.3	69.2	68.6	71.3	70.8
pPCI	2.6	2.1	2.4	3.6	6.4	9.2	10.9	12.2	13.7	15.3	17.2	20	23.3	29.6	34.1	38.9	43.2
Fibrinolytic	52.5	52.7	51.3	53.5	54.3	53.3	52	51.8	50.6	50.2	49.4	48.2	46	39.6	34.5	32.4	27.6
None	44.9	45.1	46.3	42.8	38.9	36.5	36.3	35.2	34.8	33.5	32.5	31.1	29.9	29.9	29.9	27.4	28.1

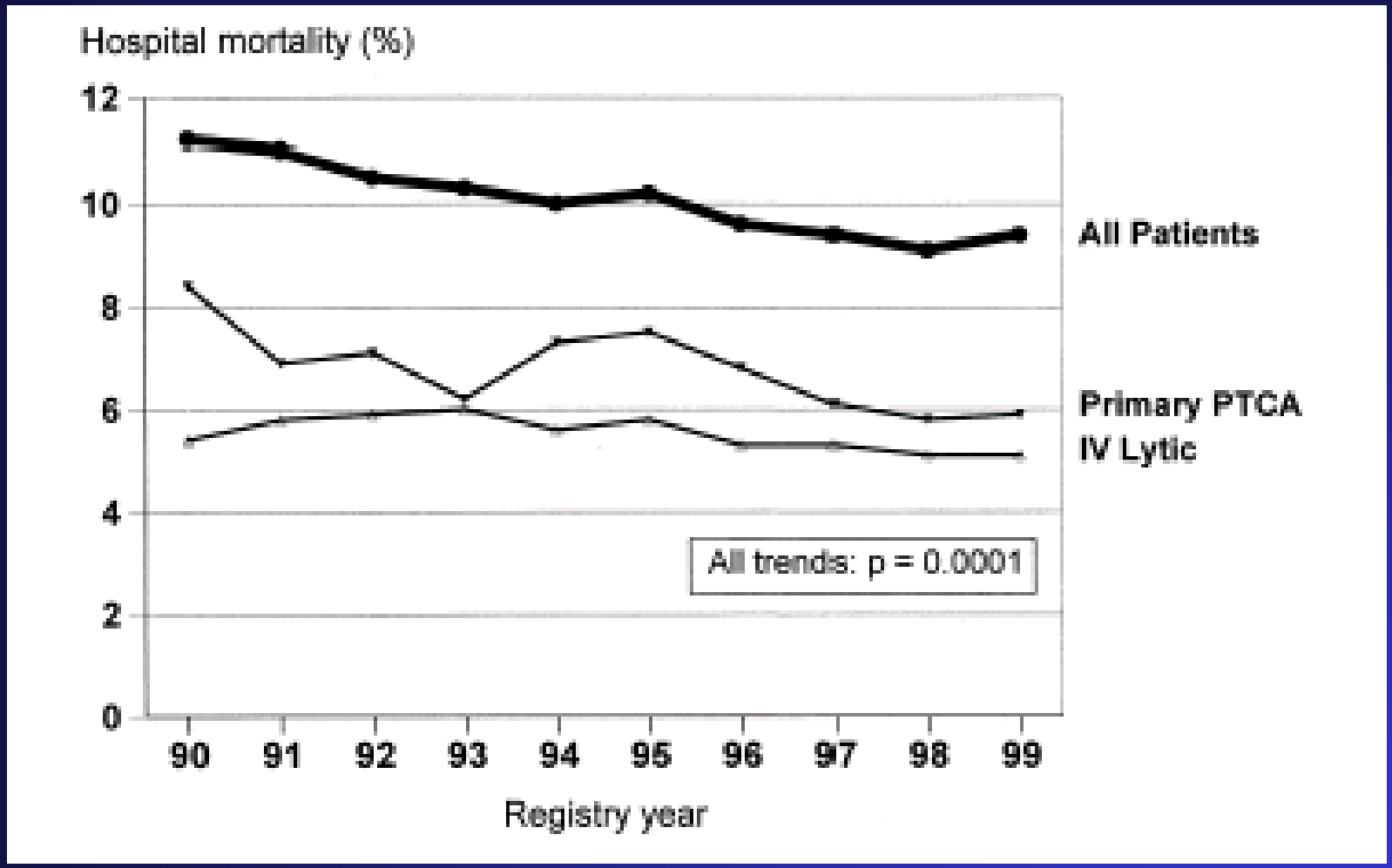
Gibson MC et al Am Heart J 2008;156:1035-1044

Reasons for not using thrombolytic therapy and direct angioplasty in TETAMI study



Cohen, M. et al. Circulation 2003;108:III-14-III-21

Hospital mortality among The National Registry of Myocardial Infarction 1, 2 and 3



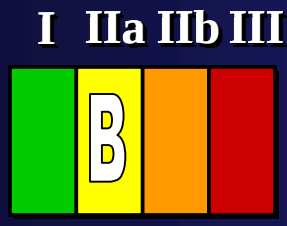
1,514,292 patients

Rogers WJ et al J Am Coll Cardiol 2000;36:2053-2063

The optimal therapy for the patient who does not receive reperfusion therapy remains to be defined.

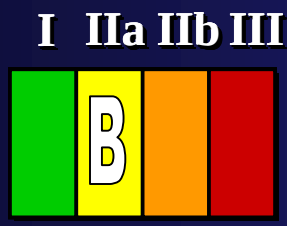
The guidelines from the ACC/AHA and ESC recommend routine use of ASA in all patients with ACS without contraindications

Anticoagulants



It is reasonable for patients with STEMI who do not undergo reperfusion therapy to be treated with anticoagulant therapy (non-UFH regimen) for the duration of the index hospitalization, up to 8 days.

Convenient strategies that can be used include those with LMWH *(Level of Evidence: C)* or fondaparinux *(Level of Evidence: B)* using the same dosing regimens as for patients who receive fibrinolytic therapy.



European Hear t Journaul. 2012

2007 Focus Update of the ACC/AHA 2004 STEMI Guidelines

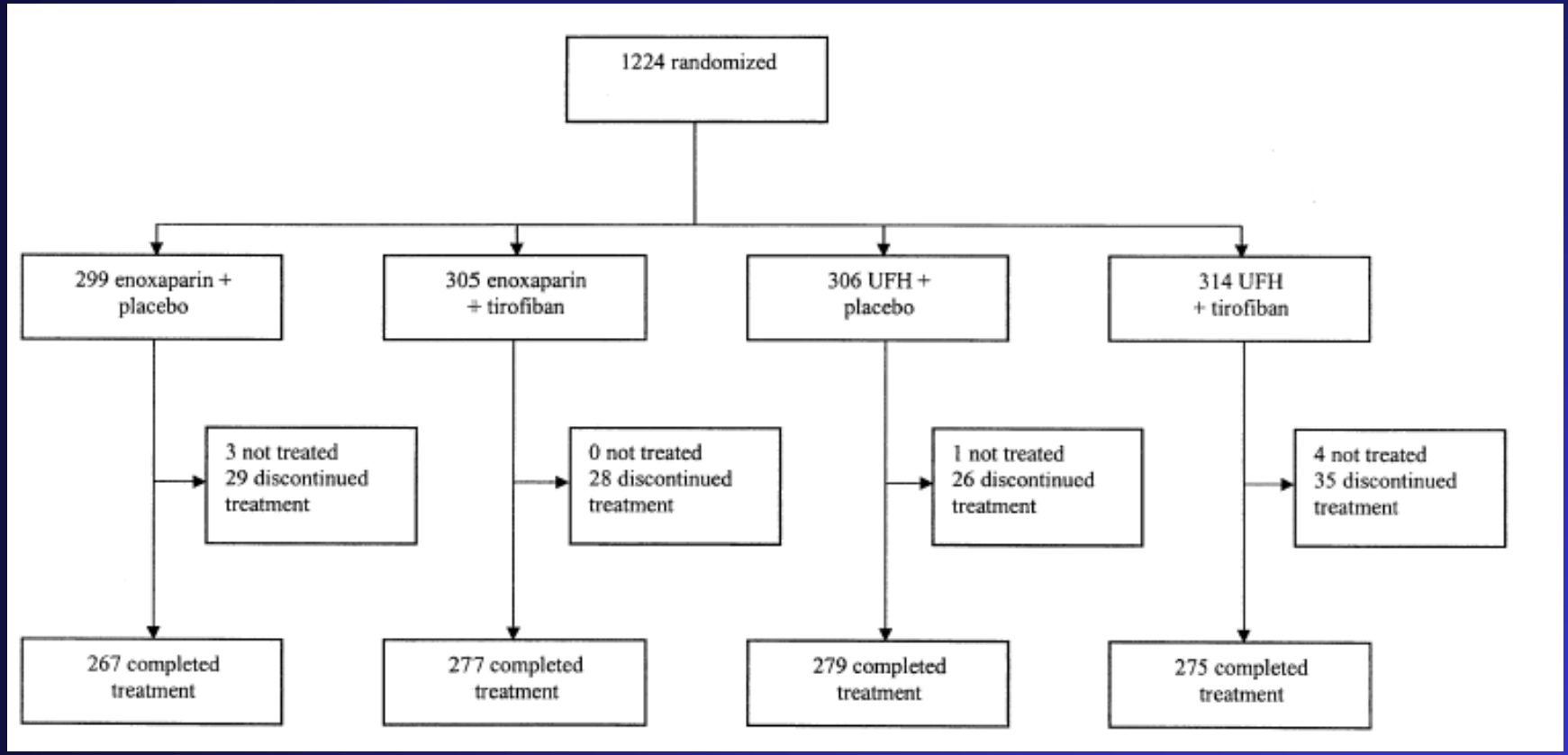
Clopidogrel 75 mg per day orally should be added to aspirin in patients with STEMI regardless of whether they undergo reperfusion with fibrinolytic therapy or do not receive reperfusion therapy.

(*Level of Evidence: A*)

Treatment with clopidogrel should continue for at least 14 days.

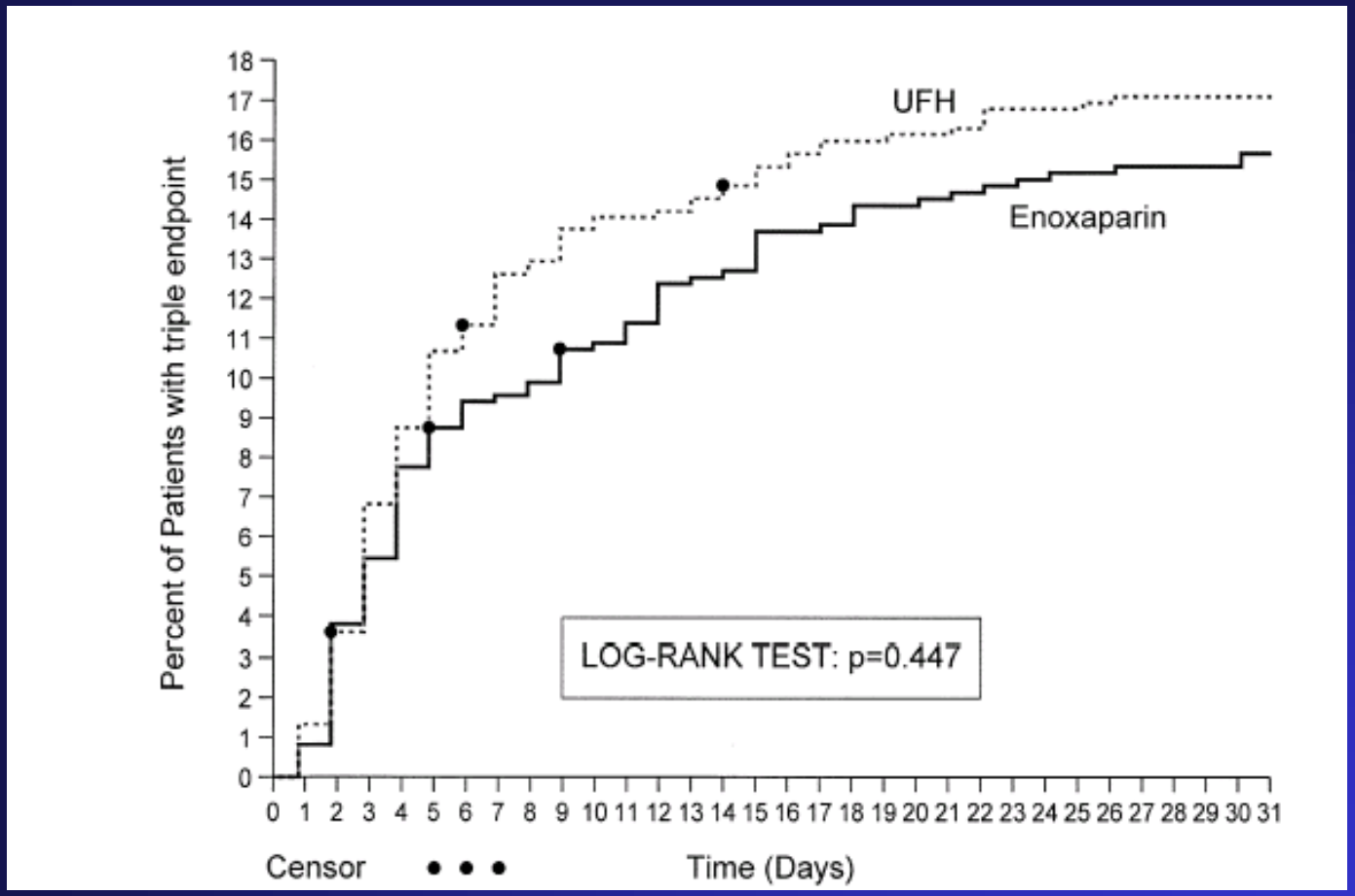
(*Level of Evidence: B*)

Prospective Evaluation of Clinical Outcomes After Acute ST-Elevation Myocardial Infarction in Patients Who Are Ineligible for Reperfusion Therapy: Preliminary Results From the TETAMI Registry and Randomized Trial



Cohen M et al. TETAMI investigators J Am Coll Cardiol 2003;42:1348-56

Time to first event for the composite triple end point in the pooled enoxaparin and UFH groups



Cohen M et al. TETAMI investigators J Am Coll Cardiol 2003;42:1348-56

OASIS-6: Study Drug Regimen and Dosing

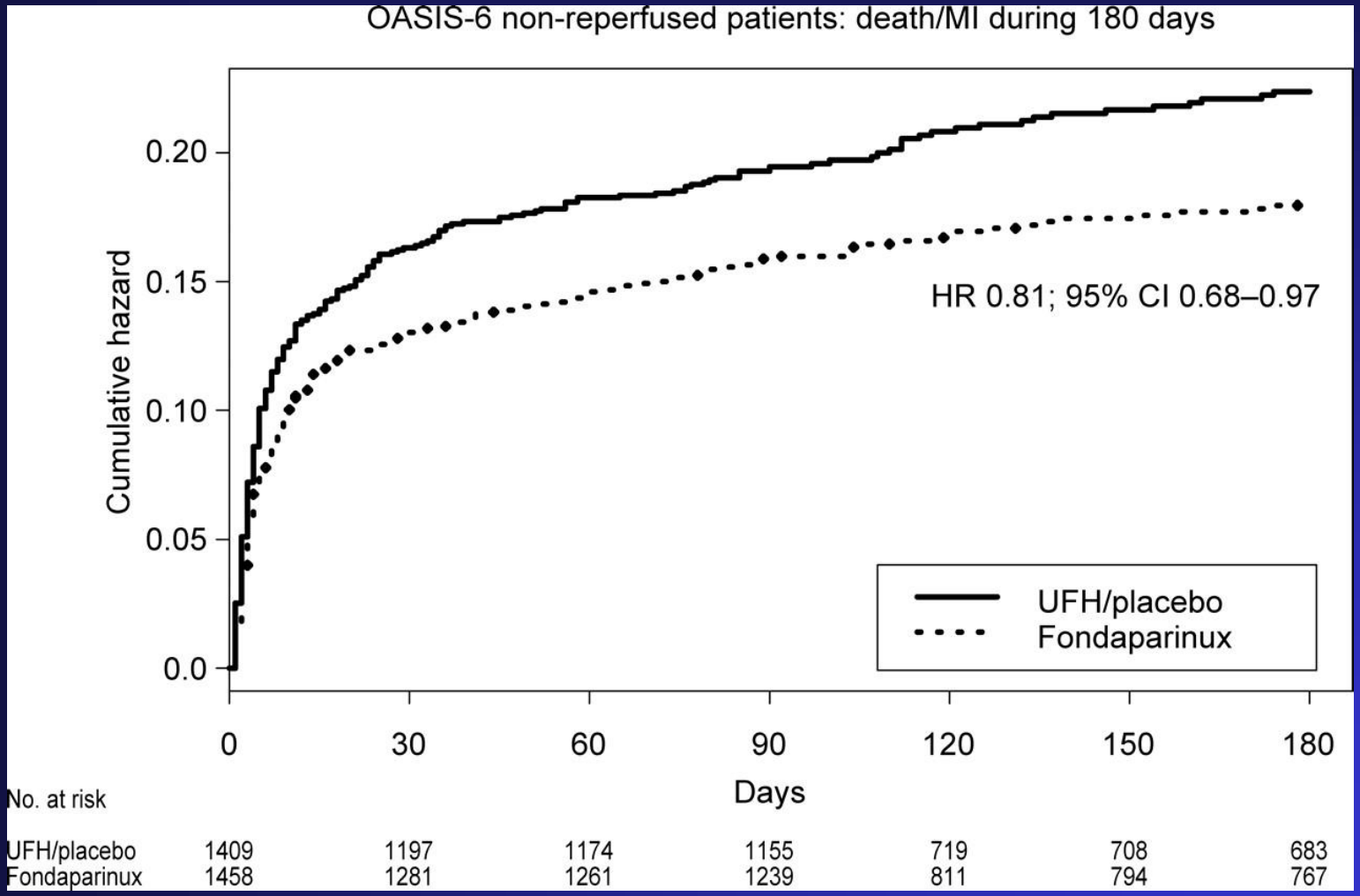
Table 1. OASIS-6: Study Drug Regimen and Dosing*

Patients Not Receiving Primary PCI		
Indication for UFH	**Fondaparinux Regimen**	**Control Regimen**
No (stratum 1)	2.5 mg subcutaneously once daily (first dose given intravenously)	Matching placebo subcutaneously once daily
Yes (stratum 2)	2.5 mg subcutaneously once daily (first dose given intravenously)†	UFH at 60 IU/kg (maximum, 4000 U) followed by intravenous infusion at 12 IU/kg/h†
Patients Scheduled for Primary PCI (Stratum 2)		
Prerandomization	**Fondaparinux Regimen**	**UFH Control Regimen**
Received UFH plus Gp IIb/IIIa antagonist	2.5-mg intravenous bolus followed by 2.5 mg subcutaneously daily for up to 8 days	Measure ACT preprocedure; UFH as per local practice (maximum, 65 IU/kg)‡
Received UFH without Gp IIb/IIIa antagonist	5.0-mg intravenous bolus followed by 2.5 mg subcutaneously for up to 8 days	Measure ACT preprocedure; UFH as per local practice (maximum, 100 IU/kg)‡
Did not receive UFH and received Gp IIb/IIIa antagonist	2.5-mg intravenous bolus followed by 2.5 mg subcutaneously daily for up to 8 days	UFH at 65 IU/kg in intravenous bolus
Did not receive either UFH or Gp IIb/IIIa antagonist	5.0-mg intravenous bolus followed by 2.5 mg subcutaneously daily for up to 8 days	UFH at 100 IU/kg in intravenous bolus

Abbreviations: ACT, activated clotting time; Gp, glycoprotein; PCI, percutaneous coronary intervention; UFH, unfractionated heparin.
*A double-blind, double-dummy technique was used for administration of all study drugs.
†If prerandomization UFH was given, study drugs were started 2 to 3 hours after the initial open-label UFH bolus or 2 to 3 hours after termination of the initial UFH infusion.
‡In patients who received UFH prior to randomization, it was recommended that an ACT be checked prior to PCI. Heparin was administered according to level of ACT, as per local practice. In those centers that did not have ACT measurement capability, it was recommended that fondaparinux, 5.0 mg intravenously, or UFH, 100 IU/kg, be given if prerandomization UFH dose was less than 4000 U and fondaparinux, 2.5 mg intravenously, or UFH, 65 IU/kg, be given if prerandomization UFH dose was 4000 to 5000 U. Patients who received more than 5000 U of prerandomization UFH were excluded from the trial.

The OASIS-6 Trial Group, JAMA 2006;295:1519-1530.*

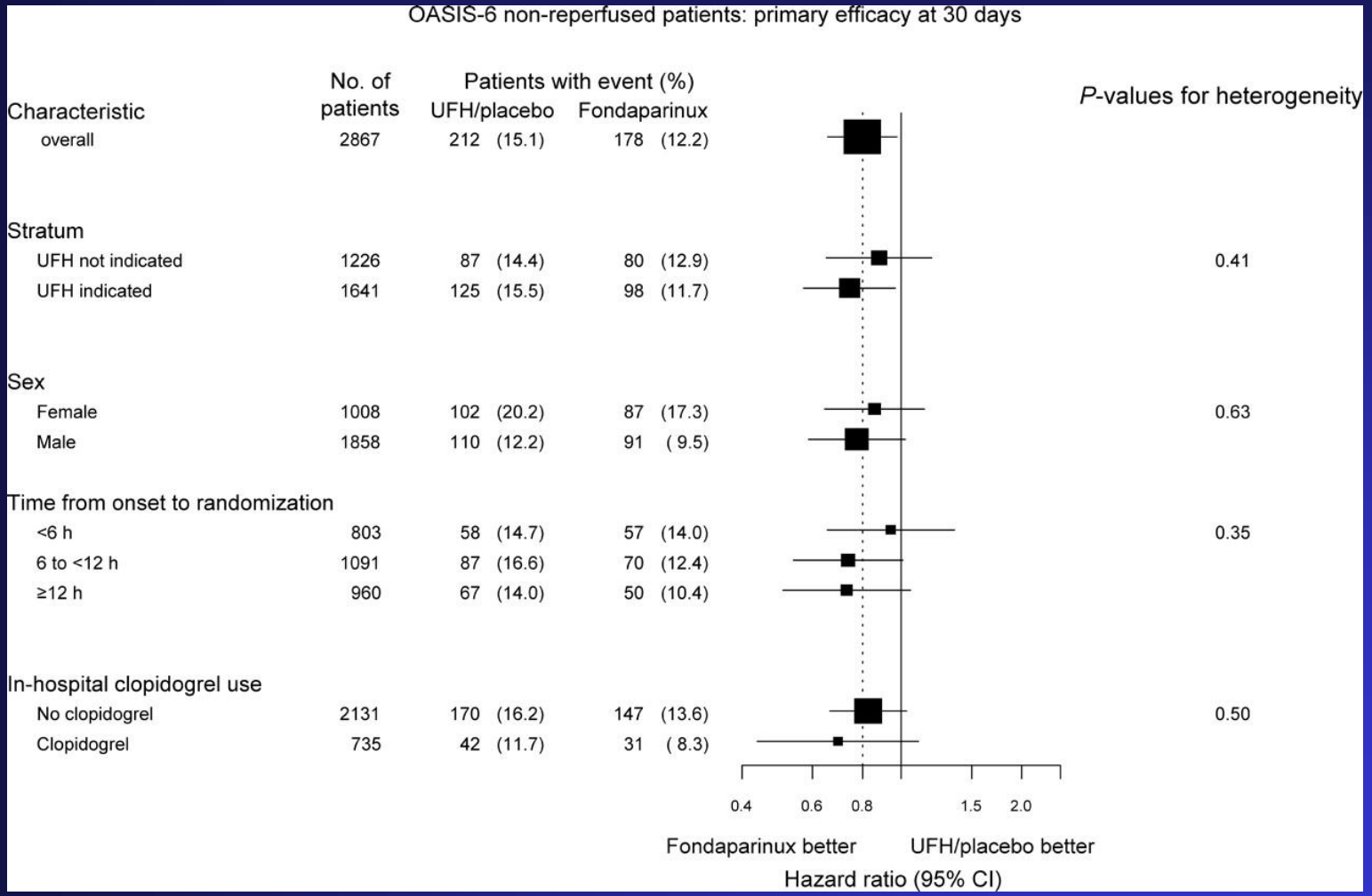
Kaplan-Meier curves with comparison of the cumulative hazard of death or myocardial re-infarction in fondaparinux and control groups



Oldgren, J. et al. Eur Heart J 2008 29:315-323

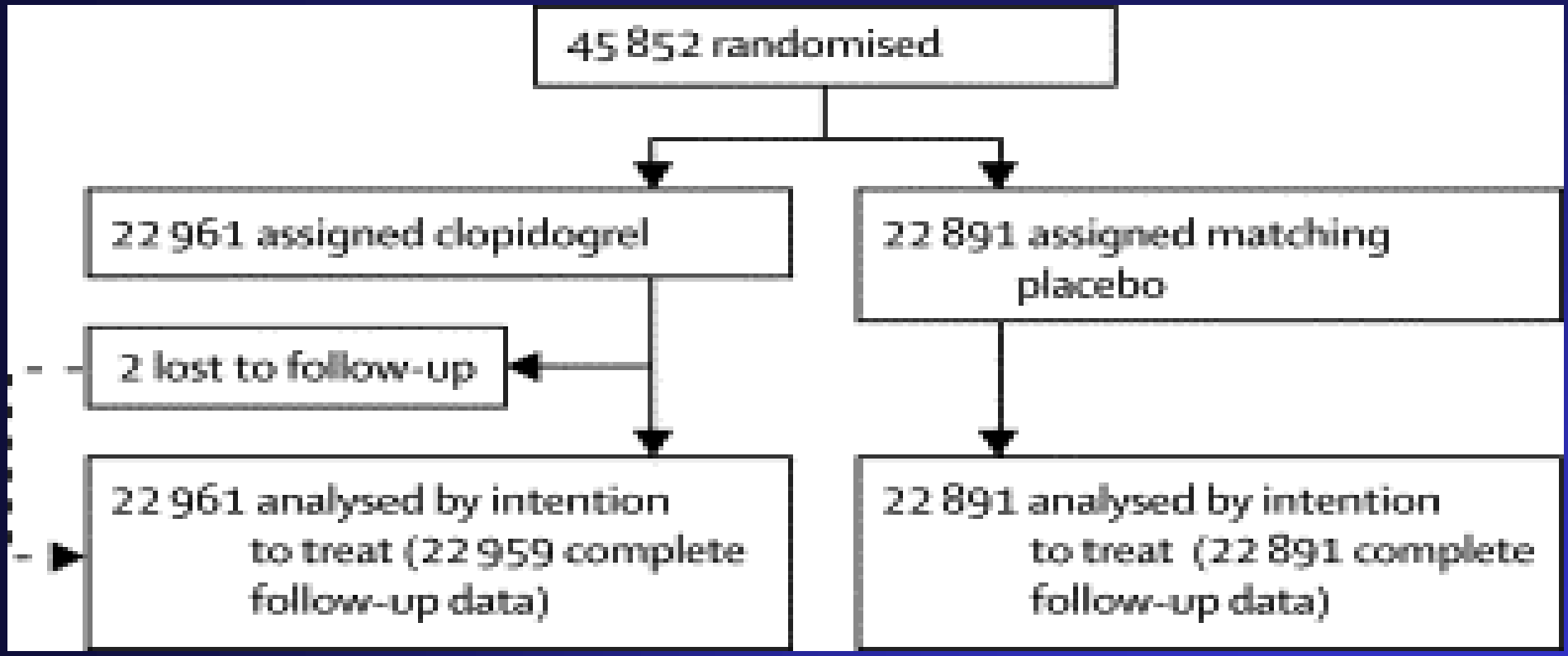
Comparison of fondaparinux vs. UFH or placebo in subgroups

Death or myocardial re-infarction



Oldgren, J. et al. Eur Heart J 2008 29:315-323

COMMIT (ClOpidogrel and Metoprolol in Myocardial Infarction Trial) collaborative group



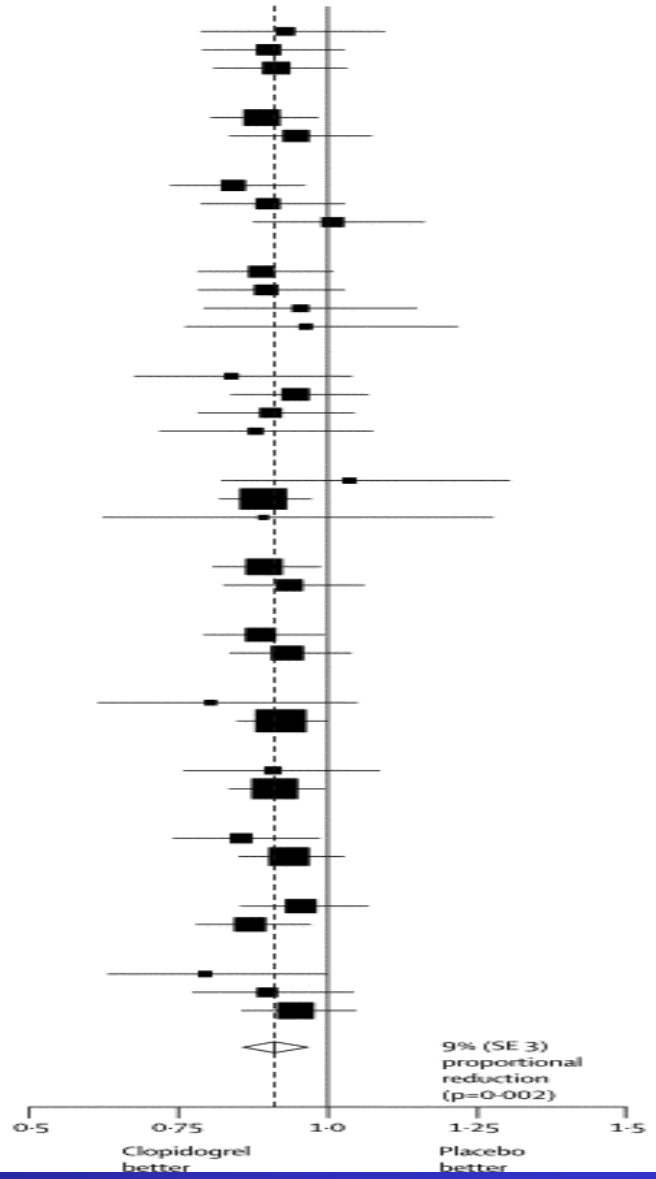
Follow-up: 28 days

Lancet. 2005;366:1607-21

COMMIT collaborative group

Baseline categorisation	Events (%) Clopidogrel (22 961)	Placebo (22 891)	Heterogeneity or trend test χ^2 (p)
Age at entry (years)			
<60	485 (5·0%)	512 (5·4%)	0·0 (0·9)
60–69	745 (10·1%)	835 (11·2%)	
⩾70	891 (14·9%)	963 (16·2%)	
Sex			
Male	1274 (7·7%)	1416 (8·6%)	1·0 (0·3)
Female	847(13·3%)	894 (14·0%)	
Time since onset (h)			
<6	709 (9·2%)	830 (10·8%)	5·7 (0·02)
6 to <13	738 (9·8%)	808 (10·8%)	
13–24	674 (8·8%)	672 (8·8%)	
Systolic blood pressure (mm Hg)			
<120	797 (10·4%)	892 (11·6%)	1·0 (0·3)
120–139	693 (8·6%)	770 (9·5%)	
140–159	388 (8·5%)	399 (8·9%)	
⩾160	243 (9·2%)	249 (9·6%)	
Heart rate (bpm)			
<70	268 (5·3%)	315 (6·2%)	0·0 (1·0)
70–89	898 (8·1%)	952 (8·5%)	
90–109	632 (12·3%)	683 (13·5%)	
⩾110	323 (19·9%)	360 (22·2%)	
ECG at entry			
Bundle branch block	270 (17·9%)	247 (17·4%)	1·8 (0·2)
ST elevation	1753 (8·8%)	1952 (9·8%)	
ST depression	98 (6·2%)	111 (7·0%)	
Killip class			
I	1273 (7·3%)	1415 (8·2%)	0·6 (0·5)
II/III	848 (15·0%)	895 (16·0%)	
Fibrinolytic agent given			
Yes	1003 (8·8%)	1122 (9·9%)	0·7 (0·4)
No	1118 (9·7%)	1188 (10·3%)	
Previous MI			
Yes	177 (9·0%)	204 (11·1%)	1·6 (0·2)
No	1944 (9·3%)	2106 (10·0%)	
Previous aspirin use			
Yes	399 (9·5%)	439 (10·4%)	0·0 (1·0)
No	1722 (9·2%)	1871 (10·0%)	
Eligible for CLARITY trial			
Yes	612 (8·2%)	717 (9·6%)	1·8 (0·2)
No	1509 (9·7%)	1593 (10·4%)	
Metoprolol allocation			
Yes	1063 (9·3%)	1110 (9·7%)	2·4 (0·1)
No	1058 (9·2%)	1200 (10·5%)	
Prognostic index (3 equal groups)			
Good	228 (3·0%)	282 (3·7%)	3·1 (0·08)
Average	574 (7·5%)	636 (8·3%)	
Poor	1319 (17·3%)	1392 (18·2%)	
Total	2121 (9·2%)	2310 (10·1%)	

Heterogeneity test: χ^2_{21}=22·9; p=0·3



Lancet. 2005;366:1607-21

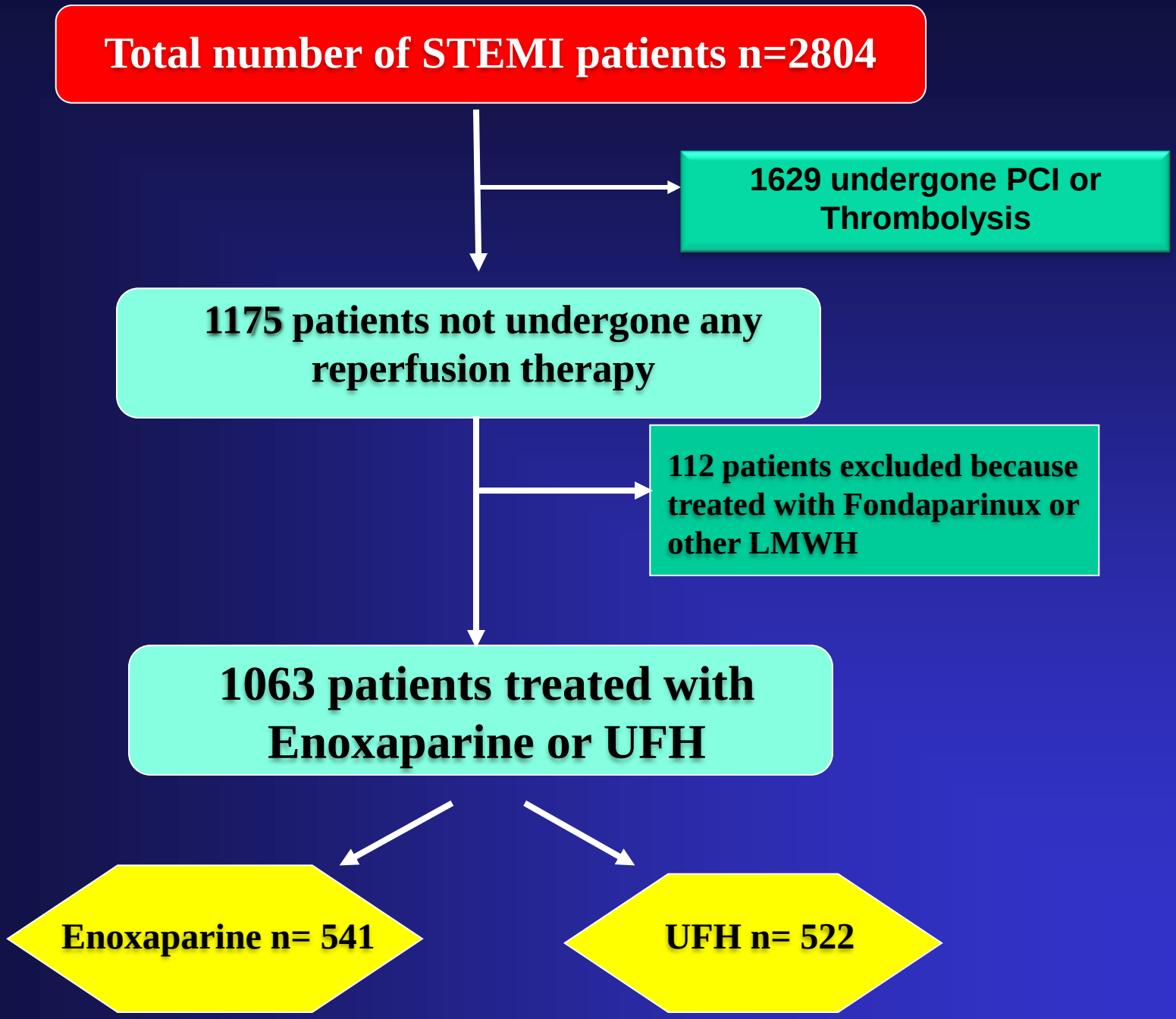
Role of observational data bases in evaluating therapy.

By design, a data base is relatively nonselective, so that the entire spectrum of patients with disease is represented. Many patients included in a clinical data base would not be included in a randomized trial.

Because a randomized trial will not be done for every subgroup, the extrapolation of trials conducted in less severely diseased patients to treatment of severely affected patients will always be an issue for debate

The main limitation of a registry-type study is the possibility of selection bias, because patients chosen to receive one therapy may differ in prognostic factors from patients chosen for an alternative therapy.

Propensity scores, which provide a scalar summary of the covariate information, do not have this limitation.. They mimic randomization in a clinical trial


Total number of STEMI patients n=2804
1629 undergone PCI or Thrombolysis
1175 patients not undergone any reperfusion therapy
112 patients excluded because treated with Fondaparinux or other LMWH
1063 patients treated with Enoxaparine or UFH
Enoxaparine n= 541
UFH n= 522

RESULTS

	Effects of UFH			Effects of Enoxaparin		
	OR	95% CI	p value	OR	95% CI	p value
Main effect models						
Unadjusted	0.63	0.45 – 0.89	0.009	1.02	0.80 – 1.56	0.504
Multivariate adjusted*	0.67	0.47 – 0.96	0.029	1.25	0.88 – 1.77	0.210
Propensity regression	0.67	0.47 – 0.96	0.027	1.25	0.88 – 1.77	0.209
Models with interactions:						
Multivariate adjusted:						
Clopidogrel users	0.62	0.41 – 0.94	0.023	0.94	0.64 – 1.37	0.745
Clopidogrel non users	0.94	0.55 – 1.60	0.819	1.64	1.05 – 2.58	0.031
Propensity regression:						
Clopidogrel users	0.66	0.43 – 0.99	0.048	1.00	0.67 – 1.48	0.996
Clopidogrel non users	0.80	0.46 – 1.40	0.437	1.53	0.96 – 2.45	0.075

Adjusted for age, sex, risk factors (dyslipidaemia, diabetes, hypertension, smoking), clinical history (prior myocardial infarction, prior angina, history of heart failure, history of stroke, previous coronary artery bypass graft, previous percutaneous coronary intervention), clinical findings (Killip class at admission, time from symptom onset to admission within 12h) and hospital treatment with antiplatelet agents (aspirin, clopidogrel).

Remarks

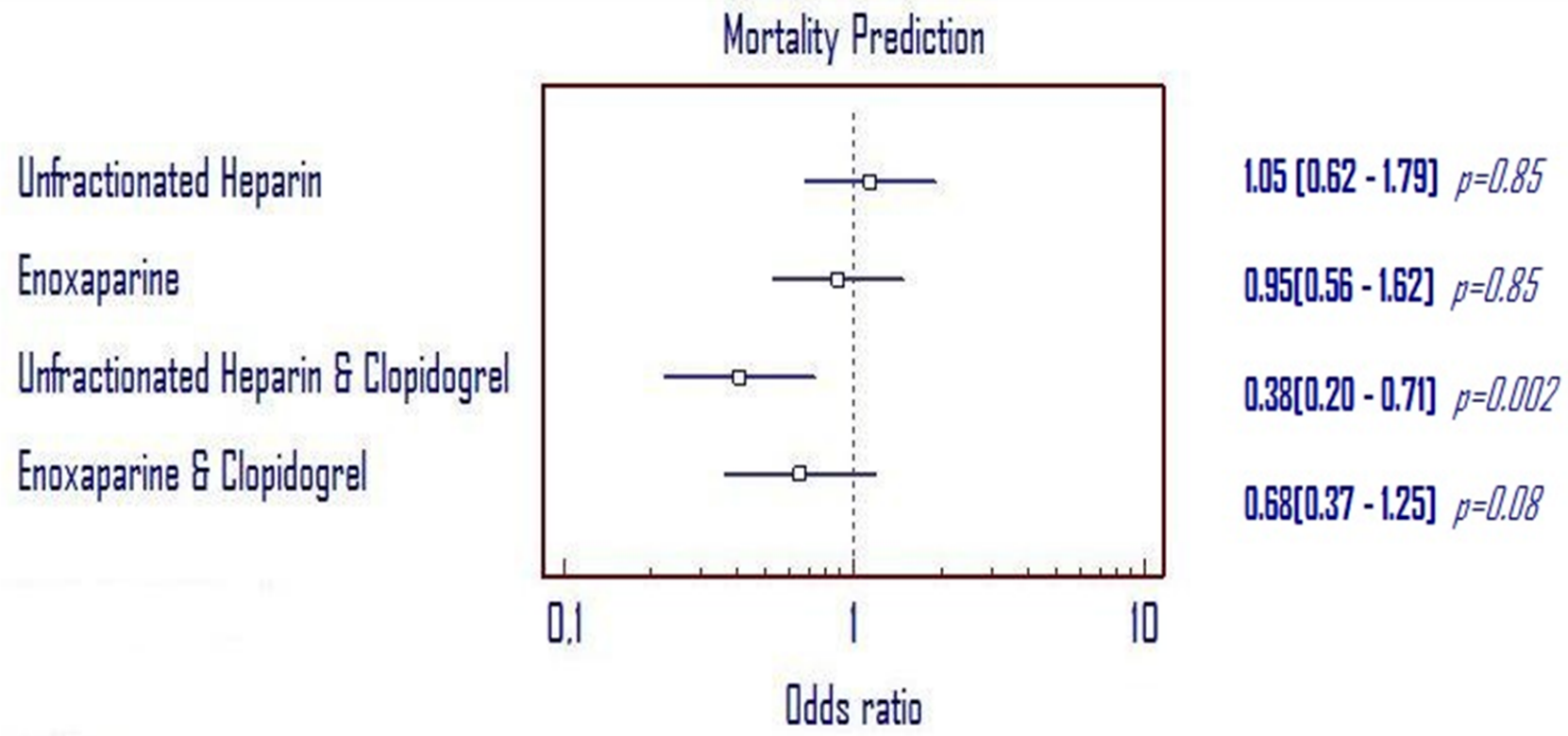
Newer antithrombotic agents, such enoxaparin, do not seem to provide reasonable alternatives to UFH in STEMI patients not undergoing reperfusion therapy.

Combined UFH-clopidogrel therapy is associated with a reduced risk of in-hospital mortality.

Propensity analyses reduce the bias to an acceptable level in observational studies.

Large-scale randomized trials are required to evaluate this therapeutic approach before its use can be recommended routinely in this patient population.

RESULTS


Mortality Prediction
Unfractionated Heparin
Enoxaparine
Unfractionated Heparin & Clopidogrel
Enoxaparine & Clopidogrel
1.05 [0.62 - 1.79] p=0.85
0.95[0.56 - 1.62] p=0.85
0.38[0.20 - 0.71] p=0.002
0.68[0.37 - 1.25] p=0.08
0,1
1
10
Odds ratio

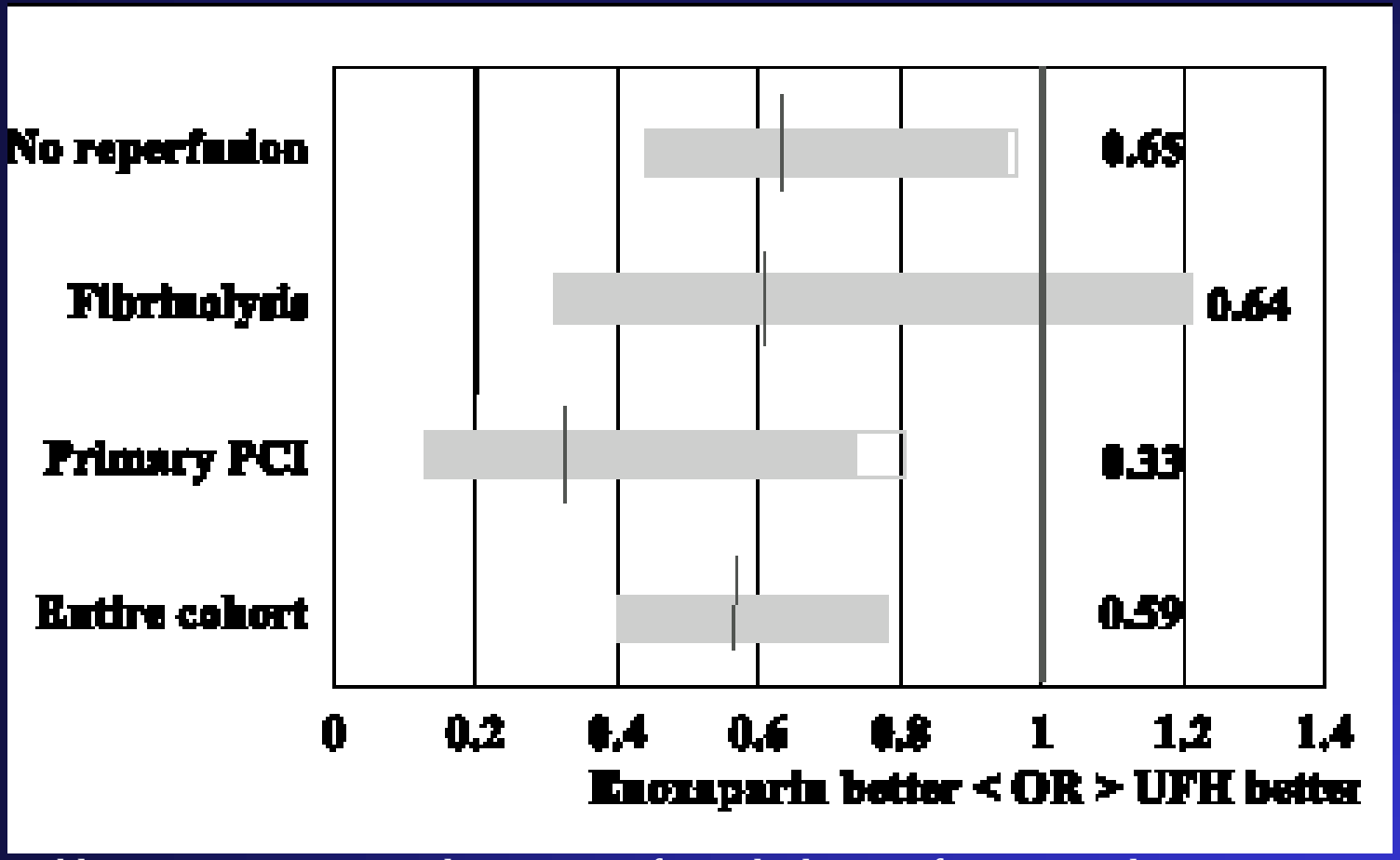
Remarks

Our results suggest that patients not receiving reperfusion therapy can be effectively and safety treated with combined UFH- clopidogrel therapy.

Well-designed, large-scale randomized trials are thus required to evaluate this therapeutic approach before its use can be recommended routinely in this patient population

Odds ratios for the combined endpoint of death and reinfarction in the multivariate analysis

Efficacy and safety of enoxaparin in unselected patients
with ST-segment elevation myocardial infarction (ACOS registry)



A multivariable propensity score analysis was performed adjusting for age, gender, prior myocardial infarction, diabetes mellitus, prior stroke, peripheral arterial disease, smoking habit, hyperlipidemia, renal insufficiency, prehospital delay and cardiogenic shock.

Zeymer U et al. Thromb Haemost 2008; 99: 150–154

Clopidogrel in addition to ASA in unselected patients with STEMI

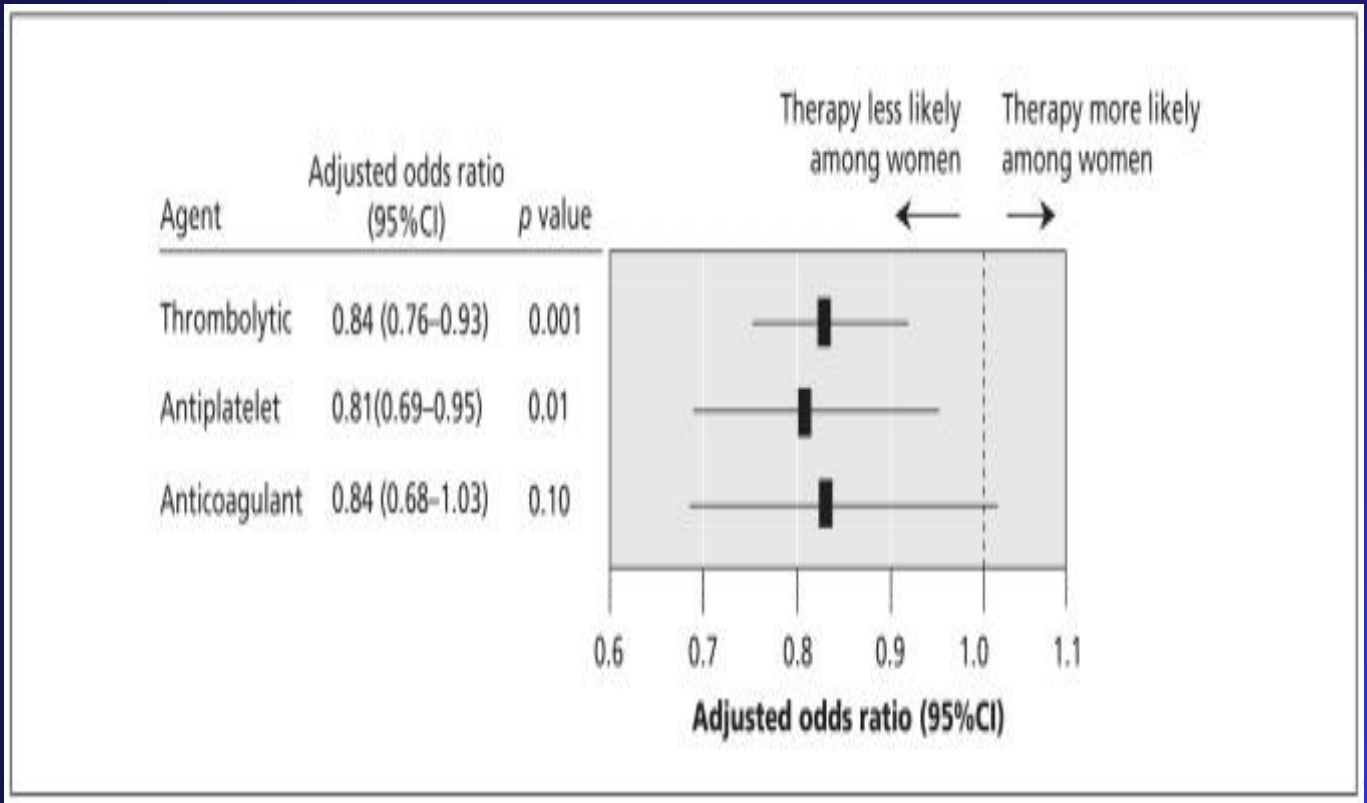
	Odds ratio	95 % Confidence interval
Mortality		
Entire group	0.65	0.42–1.00
No reperfusion	0.84	0.58–1.23
Fibrinolysis	0.83	0.52–1.33
Primary PCI	0.65	0.42–1.00
MACCE		
Entire group	0.61	0.51–0.73
No reperfusion	0.69	0.51–0.94
Fibrinolysis	0.62	0.44–0.89
Primary PCI	0.50	0.35–0.72

Odds ratios for in-hospital mortality and MACCE (death, non-fatal reinfarction and non-fatal stroke) in the multivariable analysis (age, sex, diabetes mellitus, hypertension, hyperlipidemia, prior stroke, 3-vessel disease, renal insufficiency, anterior infarct location, cardiogenic shock, reduced left ventricular function, elective revascularization, acute treatment with GP IIb/IIIa inhibitors, beta-blockers, statins, ACE-inhibitors, fibrinolysis, primary PCI and stent implantation. In the subgroup of patients treated with primary PCI stent, implantation and succesful PCI were included in the multivariate analysis**).**

(ACOS registry)

Zeymer U et al. Thromb Haemost 2008; 99: 155–160

In-hospital case fatality rates for acute myocardial infarction in Romania

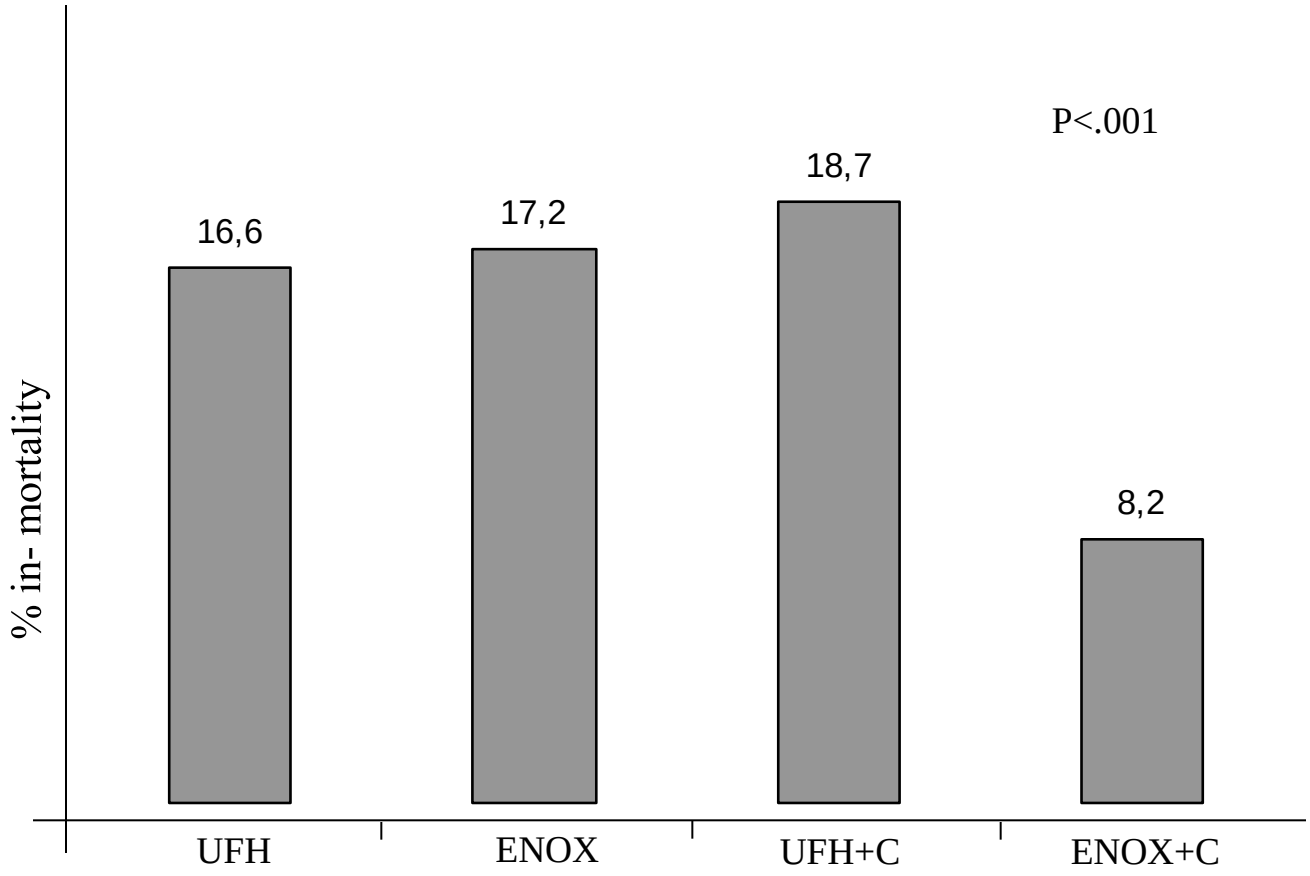


Tatu-Chitoiu G, Bugiardini R. RO-STEMI. CMAJ. 2009;180:1207-13

In-hospital case fatality rates for acute myocardial infarction in Romania

Effect of Enoxaparin	OR	(95% CI)
Main effects models		
Unadjusted	0.84	(0.7,1.01)
Multivariate adjusted*	0.71	(0.58,0.87)
Propensity regression	0.77	(0.63,0.93)
Propensity matched	0.76	(0.62,0.92)
Models with interaction		
Multivariate adjusted*		
Clopidogrel user	0.31	(0.19,0.49)
Clopidogrel nonuser	0.91	(0.73,1.14)
Propensity regression		
Clopidogrel user	0.34	(0.22,0.54)
Clopidogrel nonuser	0.92	(0.75,1.13)
Propensity matched		
Clopidogrel user	0.36	(0.22,0.59)
Clopidogrel nonuser	1.12	(0.87,1.42)

Tatu-Chitoiu G, Bugiardini R. RO-STEMI. CMAJ. 2009;180:1207-13



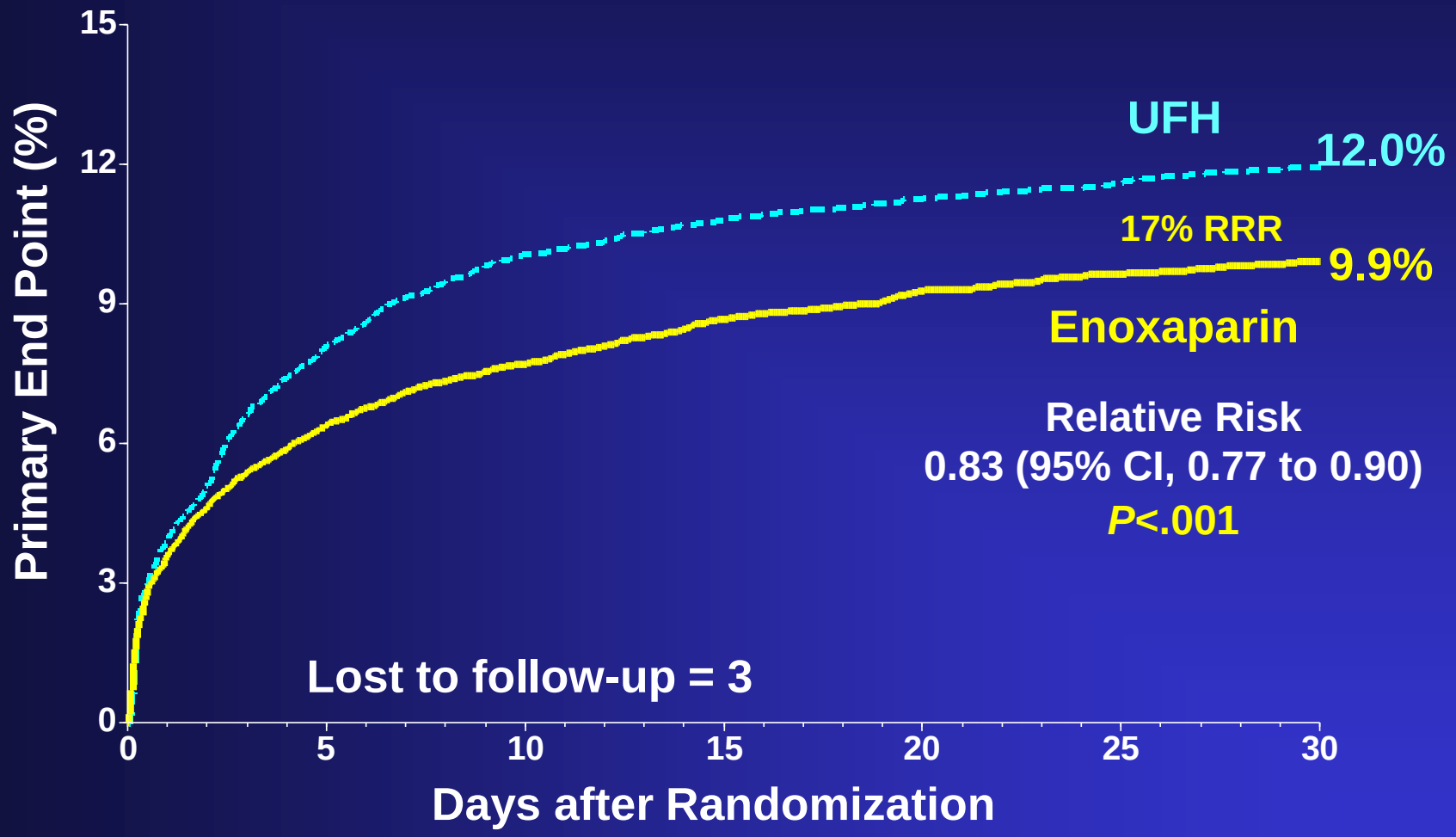
UFH = Unfractionated Heparin; ENOX = Enoxaparin; C = Clopidogrel

Tatu-Chitoiu G, Bugiardini R. RO-STEMI. CMAJ.

Characteristics of Patients

	Reperfusion Therapy		
	Yes (n=856)	No (n=584)	p-value
Age (mean, SD) – y	60.3±12.6	67.3±13.1	<0.001
Male, n (%)	620/856 (72.4)	368/584 (63.0)	<0.001
History of lipid disorders, n (%)	151/617 (24.5)	122/463 (26.4)	0.48
History of diabetes, n (%)	193/799 (24.2)	150/541 (27.8)	0.19
History of hypertension, n (%)	456/834 (54.7)	338/571 (59.2)	0.09
Current smoker, n (%)	356/834 (42.7)	194/565 (34.3)	<0.01
Prior myocardial infarction, n (%)	94/849 (11.1)	87/577 (15.1)	0.03
Presentation characteristics, Killip class ≥2, n (%)	209/744 (28.1)	117/313 (37.4)	<0.01
Time from symtom onset to admission, 6-12 h, n (%)	165/856 (19.3)	197/584 (33.7)	<0.001

ExTRACT-TIMI 25: Primary End Point (ITT) Death or Nonfatal MI



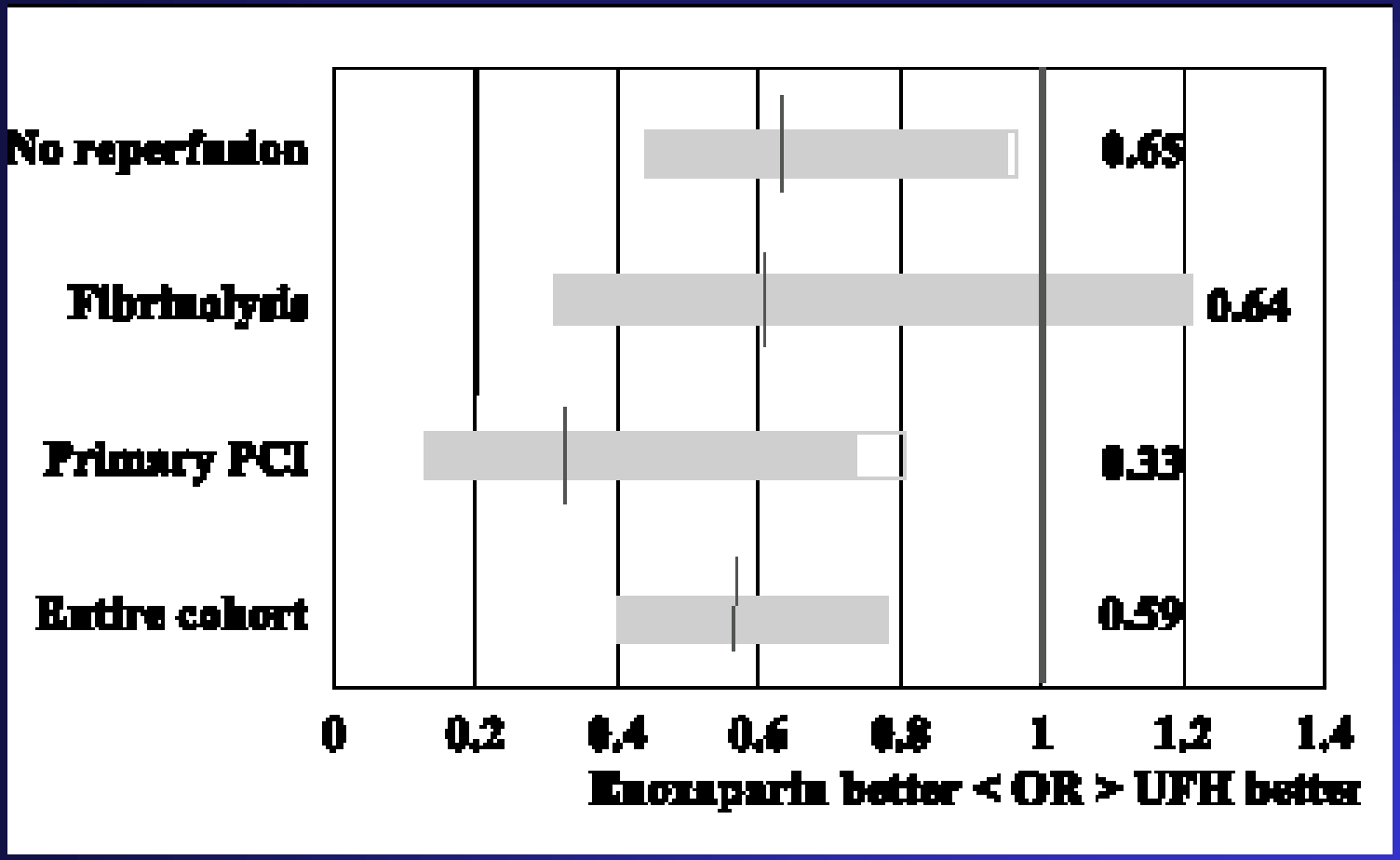
Antman EM, et al. N Engl J Med. 2006;354:1477-1488.

We reviewed current practices in antithrombotic therapy with enoxaparin versus unfractionated heparin of patients with STEMI who did not undergo any form of coronary reperfusion in the Romanian registry of acute myocardial infarction (RO-STEMI).

The rural inhabitants in Romania represent more than 50% of the overall population. The chances of a rural patient to achieve thrombolysis or primary percutaneous intervention are compromised by isolation and lack of resources.

Odds ratios for the combined endpoint of death and reinfarction in the multivariate analysis

Efficacy and safety of enoxaparin in unselected patients with ST-segment elevation myocardial infarction



Zeymer U et al. Thromb Haemost 2008; 99: 150–154

Recent trials comparing use of prolonged anticoagulation therapy with new agents versus unfractionated heparin in ST-segment elevation myocardial infarction (STEMI) have yielded robust efficacy and safety results than have earlier trials.

Based on these findings, the current guidelines of the American College of Cardiology and the American Heart Association recommend the use of reviparin, enoxaparin or fondaparinux along with any fibrinolytic agents in clinical use, yet after percutaneous coronary intervention.

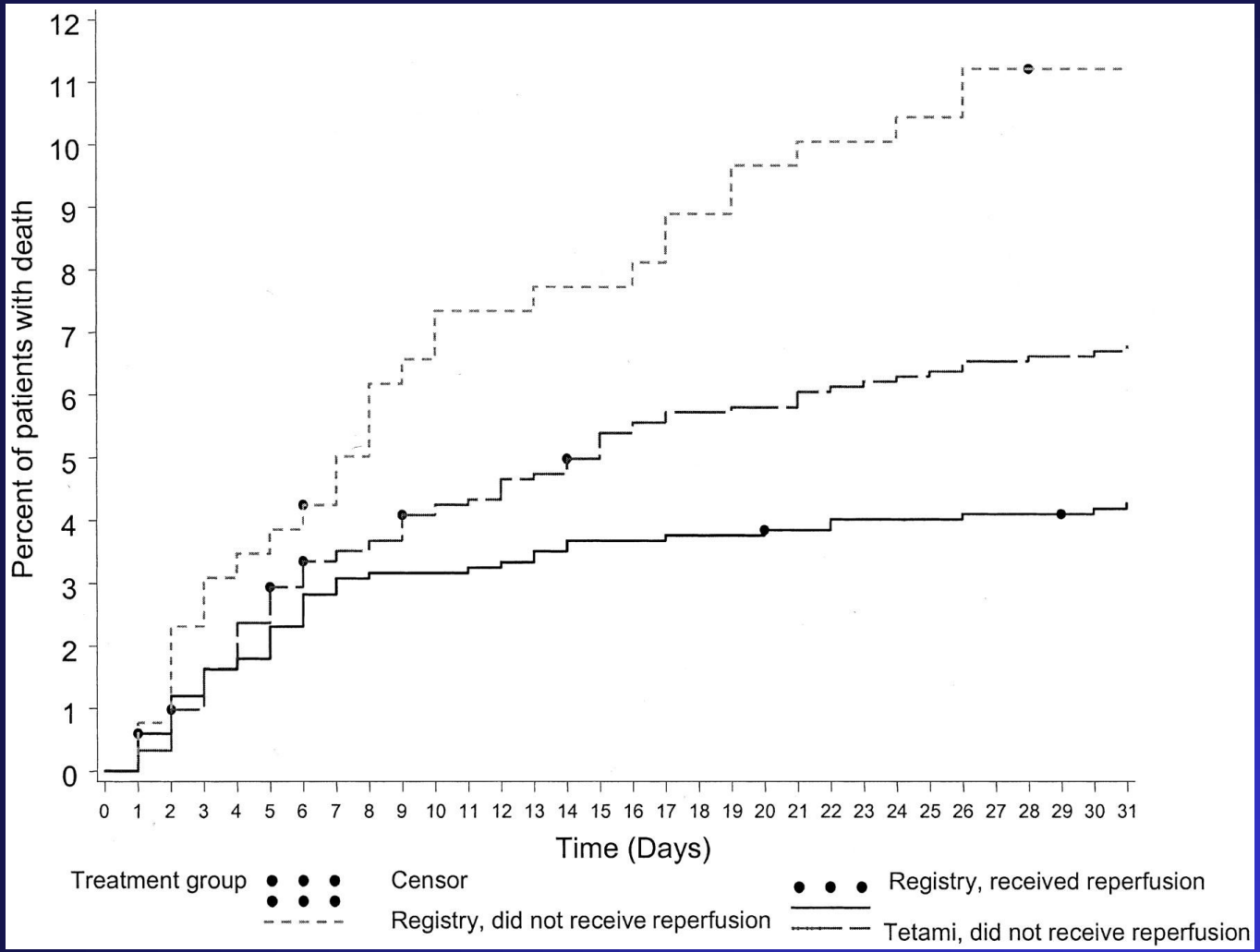
Prospective Evaluation of Clinical Outcomes After Acute ST-Elevation Myocardial Infarction in Patients Who Are Ineligible for Reperfusion Therapy: Preliminary Results From the TETAMI Registry and Randomized Trial

	All (N = 1,224)	Enoxaparin/Placebo (n = 299)	Enoxaparin/Tirofiban (n = 305)	UFH/Placebo (n = 306)	UFH/Tirofiban (n = 314)
Baseline characteristics					
Mean age (yrs)	62.8	62.4	62.9	62.5	63.2
Patients (%)					
Male	72.4	72.2	75.4	71.6	70.4
Anterior MI	44.7	46.8	41.6	45.1	45.2
Killip class I	85.8	87.6	85.9	82.4	87.3
Killip class II	13.2	11.4	13.1	16.7	11.8
Killip class III	1.0	1.0	1.0	1.0	1.0
ECG characteristics					
Any ST-segment elevation	86.8	83.9	90.2	86.9	86.0
Q-wave MI	68.1	70.2	69.5	66.3	66.6
Conduction abnormalities	12.7	13.4	10.5	13.7	13.1

ECG = electrocardiography; MI = myocardial infarction; UFH = unfractionated heparin.

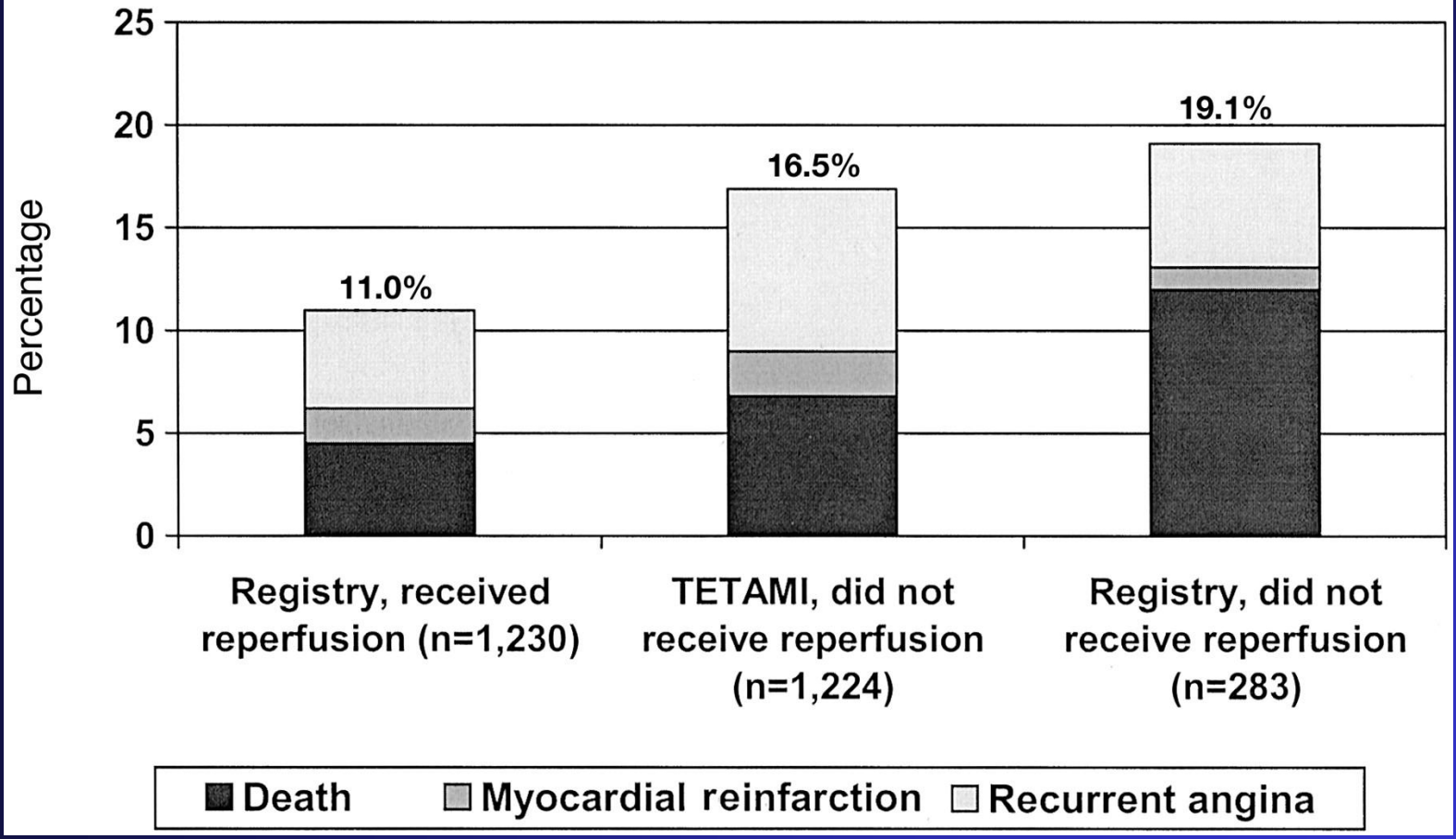
Cohen M et al. TETAMI investigators J Am Coll Cardiol 2003;42:1348-56

Time to death at 30 days by reperfusion status



Cohen, M. et al. Circulation 2003;108:III-14-III-21

Clinical event rates at 30 days, by reperfusion status



Cohen, M. et al. Circulation 2003;108:III-14-III-21

Conclusions From the TETAMI Registry

The TETAMI registry found that patients who received early reperfusion had lower clinical event rates at 30 days, compared with patients who did not receive reperfusion therapy. In particular, 30-day mortality was only 4.4% in patients who received reperfusion therapy, compared with 12% in non-TETAMI patients who did not receive reperfusion therapy.

Mortality in the TETAMI randomized study group was intermediate.

Cohen M et al. TETAMI investigators J Am Coll Cardiol 2003;42:1348-56

Baseline characteristics

	Enoxaparin (n=1462)	UFH (n=2350)	p-value
Age (mean, SD) – y	66.0 ± 13.4	65.6 ± 12.2	0.36
Male, n (%)	913/1462 (62.4)	1449/2350 (61.7)	0.66
History of lipid disorders, n (%)	612/1448 (42.3)	692/2349 (29.5)	<0.0001
History of diabetes, n (%)	378/1462 (25.8)	547/ 2350 (23.3)	0.08
History of hypertension, n (%)	880/1462 (60.1)	1214/2350 (51.7)	<0.0001
Current smoker, n (%)	655/1462 (44.8)	974/2350 (41.5)	<0.05
Prior myocardial infarction, n (%)	197/1462 (13.4)	211/2349 (9.0)	<0.0001
Presentation characteristics, n (%)			
Anterior acute myocardial infarction	727/1462 (49.7)	1196/ 2350 (50.9)	0.47
Killip class ≥2	705/1449 (48.6)	807/ 2350 (34.3)	<0.0001
Time to treatment >12 hours, n (%)*	577/1304 (44.2)	537/1579 (34.0)	<0.0001
Medication, n (%)			
Aspirin	1346 /1461 (92.1)	1939/2350 (82.5)	<0.0001
Clopidogrel	438/1461 (29.9)	337/2350 (14.3)	<0.0001
Aspirin and/or clopidogrel	1369 /1461 (93.7)	1961 /2350 (83.5)	<0.0001
Outcomes, n (%)			
Death	212/1462 (14.5)	397/ 2350 (16.9)	<0.05
Non fatal intracranial haemorrhage	10/1449 (0.7)	18/2346 (0.8)	0.42

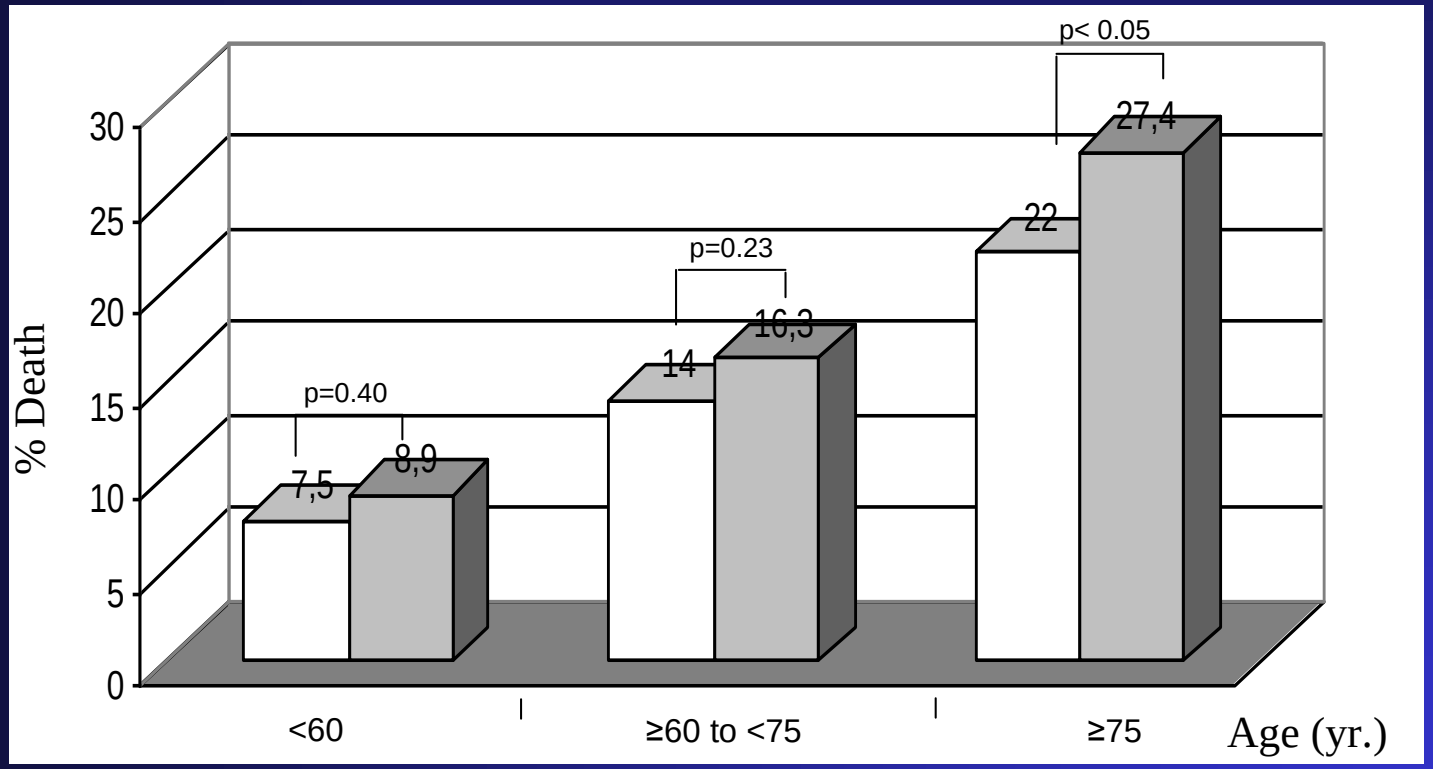
*Data available for 2883 (75.8%) patients; UFH, unfractionated heparin.

Baseline characteristics of patients according to age groups

	Age groups			
	<60 (n=1174)	≥60 to 74 (n=1567)	≥75 (n=1071)	p-value
Male, n (%)	940/1174 (80.0)	954/1567 (60.8)	468/1071 (43.6)	<0.0001
History of lipid disorders, n (%)	485/1169 (41.5)	514/1562 (32.9)	305/1066 (28.6)	<0.0001
History of diabetes, n (%)	256/1174 (21.8)	422/1567 (26.9)	247/1071 (23.0)	<0.01
History of hypertension, n (%)	533/1174 (45.4)	920/1567 (58.7)	641/1071 (59.8)	<0.0001
Current smoker, n (%)	785/1174 (66.8)	616/1567 (39.3)	228/1071 (21.2)	<0.0001
Prior AMI, n (%)	107/1174 (9.1)	184/1566 (11.7)	117/1071 (10.9)	0.06
Presentation characteristics, n (%)				
Anterior AMI	581/1174 (49.4)	784/1567 (50.0)	558/1071 (52.1)	0.42
Killip class ≥2	387/1170(33.1)	602/1561(38.6)	523/1068(48.9)	<0.0001
Time to treatment >12 hrs, n (%) *	352/883 (39.9)	456/1148 (39.7)	306/852 (35.9)	0.15
Medication, n (%)				
Aspirin	1009/1174 (85.9)	1362/1567 (86.9)	914/1070 (85.4)	0.52
Clopidogrel	342/1174 (29.1)	296/1567 (18.8)	137/1070 (12.8)	<0.0001
Aspirin and/or clopidogrel	1024/1174(87.2)	1380/1567 (88.0)	926/1070 (86.5)	0.50
Outcomes, n (%)				
Death	97/1174 (8.3)	241/1567(15.4)	271/1071 (25.3)	<0.0001
Non fatal intracranial haemorrhage	6/1170 (0.5)	9/1560 (0.6)	13/1065 (1.22)	0.79

*Data are available for 2883 (75.8%) patients; AMI, acute myocardial infarction

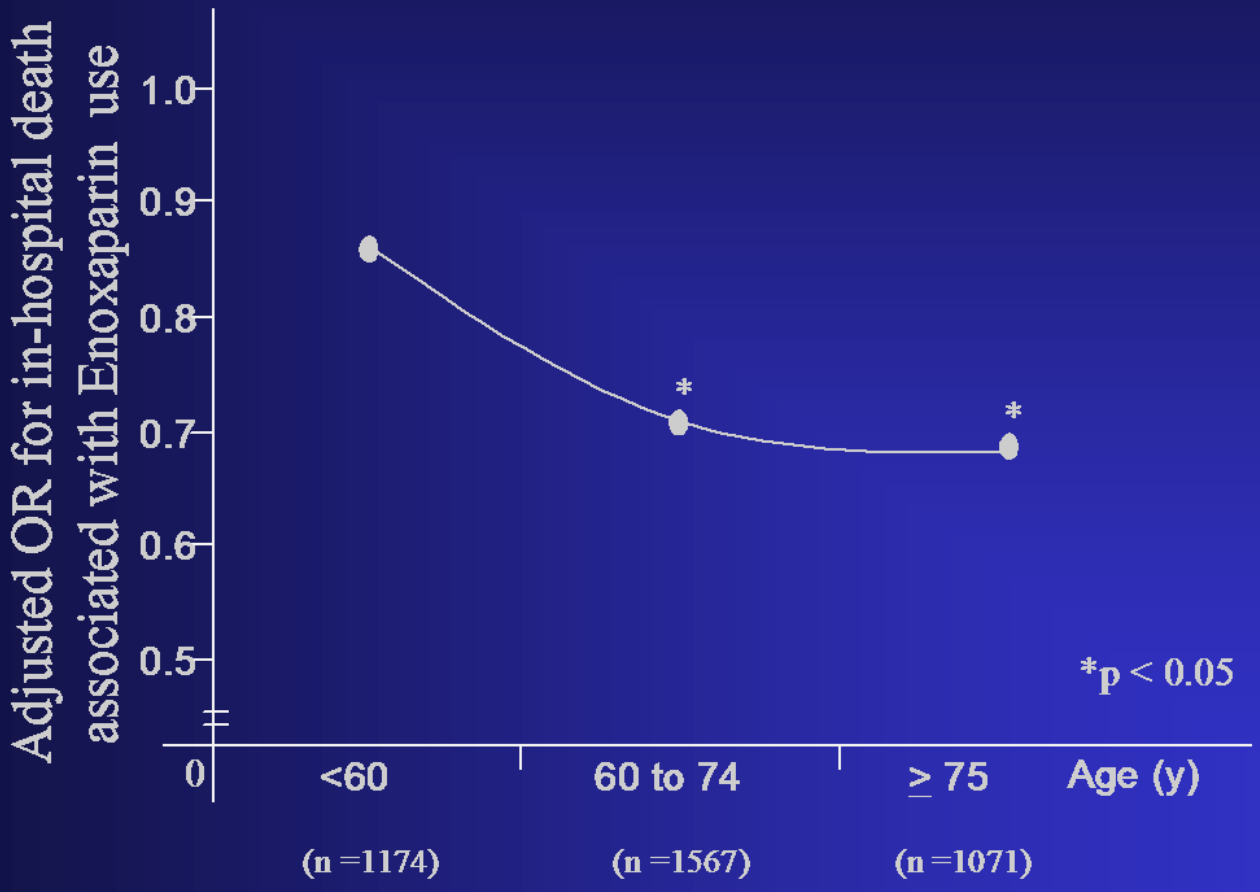
Death according to age group and treatment



(n = 1174) (n = 1567) (n = 1071)

Submitted to J Am Coll Cardiol

Death according to age in enoxaparin group



Submitted to J Am Coll Cardiol

Conclusions

In RO-STEMI, a large proportion of patients did not undergo reperfusion therapies. In this registry, patients had greater absolute and relative risk reductions of mortality when treated with enoxaparin up to 8 days compared with unfractionated heparin given for a median of 72 hours from admission.

The risk of intracranial hemorrhage was not increased by enoxaparin.

In addition, this analysis found significant age-by-treatment relation in mortality according to antithrombotic treatment, with older people being higher risk and more likely to benefit from enoxaparin.

APPENDIX

IRACS-CT Administrative Committee:

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Eva Goncalvesova and Martin Studenkan (Slovakia)

CONCLUSIONS

- **Observational studies do not control for unmeasured differences in patient characteristics. Propensity analyses reduce the bias to an acceptable level**
- **Combined UFH-clopidogrel therapy was associated with a reduced risk of in-hospital mortality. Benefits were consistent across all age groups**

International Survey of Acute Coronary Syndromes in Transitional Countries

- Bosnia and Herzegovina
- Bulgaria
- Croatia
- Hungary
- Italy
- Poland
- Romanian
- Russian Federation
- Serbia and

- Latvia
- Lithuania