

Speaker's Name

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In-ambulance abciximab administration in STEMI patients undergoing primary PCI is associated with smaller infarct size, improved LV function and lower incidence of heart failure: Results from the Leiden MISSION! infarct treatment optimization program

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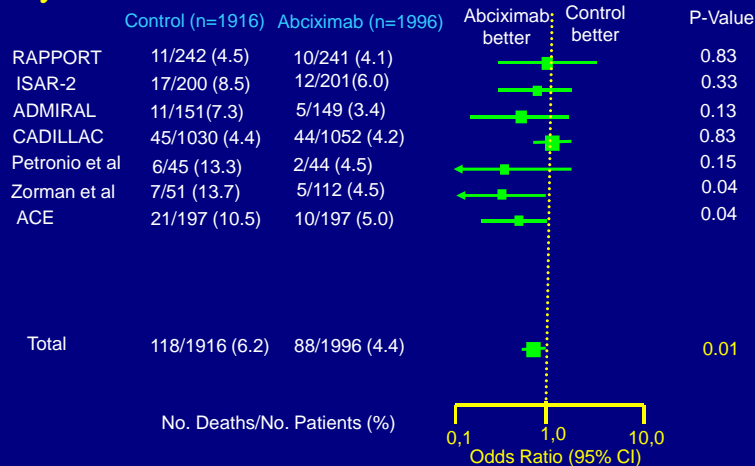
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Adjunctive abciximab has been shown to reduce mortality in STEMI patients undergoing PPCI

Mortality 6 Months



De Luca et al. JAMA 2005;293:1759-1765

ESC Guidelines for STEMI

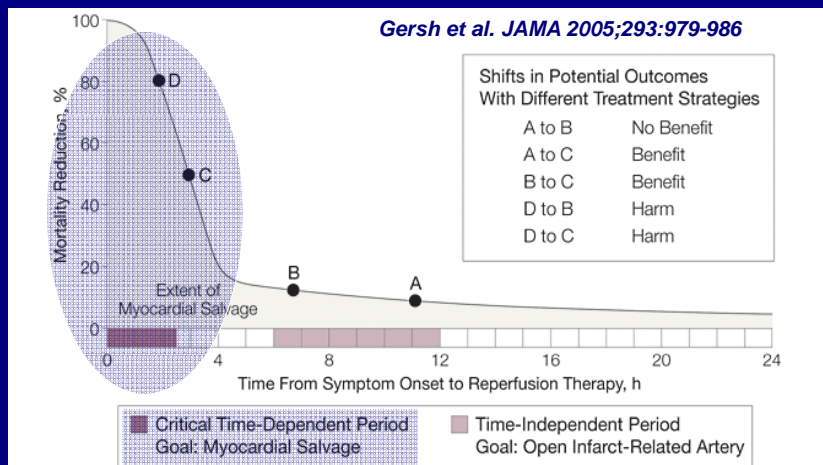
Recommendation for use of Abciximab in PCI for STEMI

Procedure	Indication	Recommendation	Studies for Level A or B
Abciximab	All Primary PCI (preferably in high risk patients)	Ila A	ADMIRAL, ACE

However, optimal timing of administration remains under investigation.

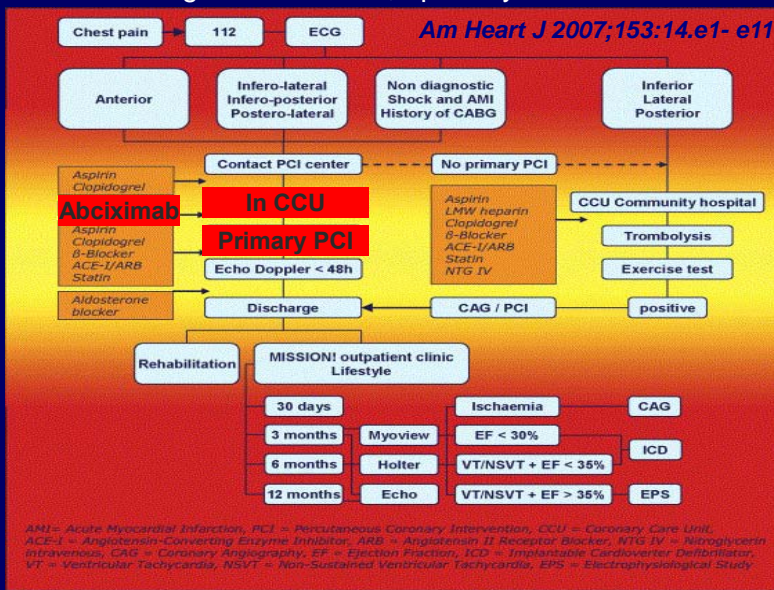
Silber et al. EHJ 2008; 26:804-847

The most critical point for PPCI is TIME
GOLDEN PERIOD for myocardial salvage is first 2 hrs



Is early abciximab administration important?

The **MISSION! protocol** is a rigorously standardized protocol. Contains a pre-hospital, in-hospital, and outpatient clinical framework for decision making and treatment, up to 1 year after the index event.



Aim of our study

Evaluate the effects of early (in-ambulance) versus late (in-hospital) administration of abciximab on immediate, short and long term outcomes.

STUDY GROUPS

December 2006

MISSION protocol

STEMI patients undergo PPCI with abciximab pre-treatment

Late Group

Abciximab in-hospital
N= 90

Inclusion criteria:

- Symptom duration < 9 hours,
- ECG with clear ST-segment elevation and
- Receive abciximab prior to PPCI.

Exclusion criteria :

LBBB and contraindications for abciximab, aspirin, clopidogrel or heparin.

Early Group

Abciximab in-ambulance
N= 89

END POINTS OF THE STUDY

Primary angiographic end point

Early reperfusion (TIMI 2 or 3 flow) in the IRA before angioplasty.

Secondary end points

Electrocardiographic

ST-segment deviation resolution ($\geq 70\%$) at 90 min post-PPCI.

Enzymatic Infarct size

In the first 48h by cumulative release of CK.

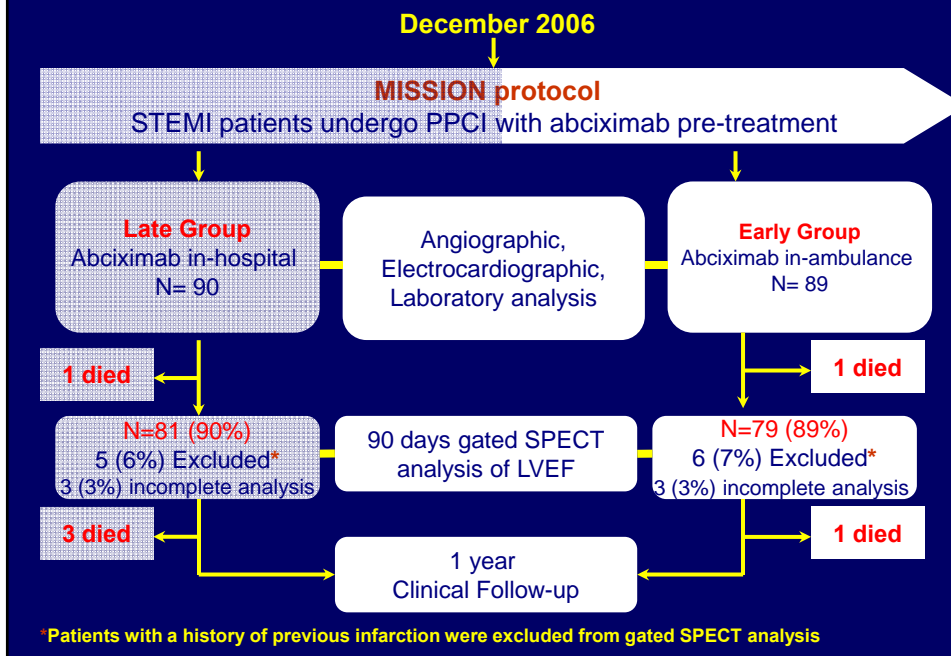
LV ejection fraction (LVEF)

At 90 days after PPCI evaluated by ECG gated SPECT at rest using Technetium-99m Tetrofosmin.

Clinical outcome (MACE)

In a dedicated out-patient clinic at 1, 3, 6 and 12 months.

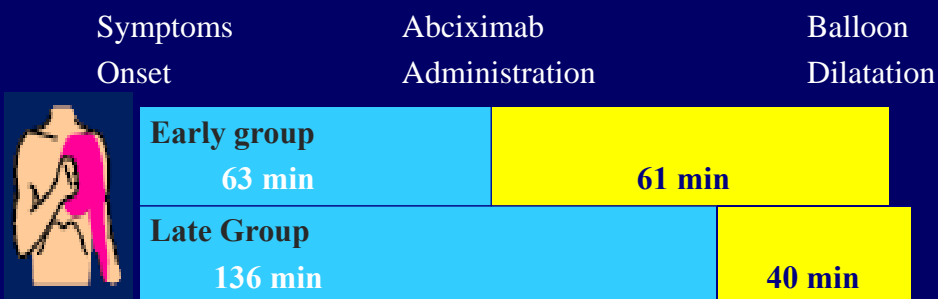
FLOW CHART OF THE STUDY



Baseline characteristics of the study population

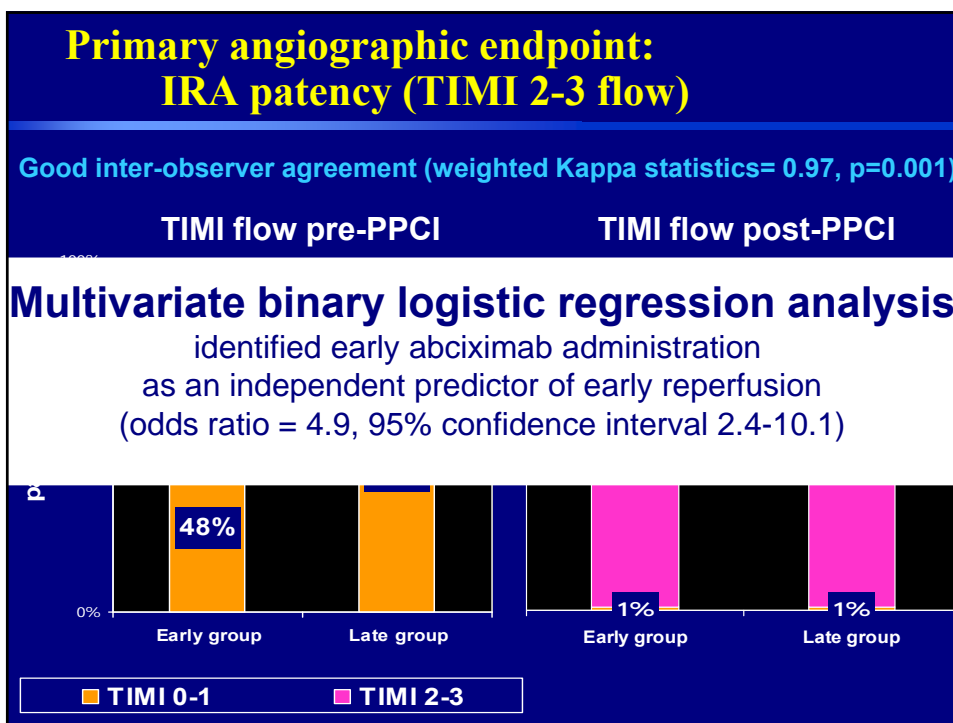
	Early group (n= 89)	Late group (n= 90)	<i>P</i>
Age (years)	61±11	59 ±12	NS
Age ≥75 yrs, n (%)	15 (17)	11 (12)	NS
Male gender, n (%)	65 (74)	75 (83)	NS
Risk factors, n (%)			
Previous MI	6 (7)	5 (6)	NS
Hypertension	36 (40)	27 (31)	NS
Diabetes mellitus	11 (12)	10 (11)	NS
Hypercholesterolemia	40 (45)	38 (43)	NS
Current Smoking	57 (64)	47 (54)	NS
Positive Family history	40 (45)	38 (43)	NS
Killip class ≥ 2, n (%)	3 (4)	6 (7)	NS
Site of MI, n (%)			
Inferior MI	49 (55)	44 (49)	NS
Anterior MI	40 (45)	46 (51)	NS

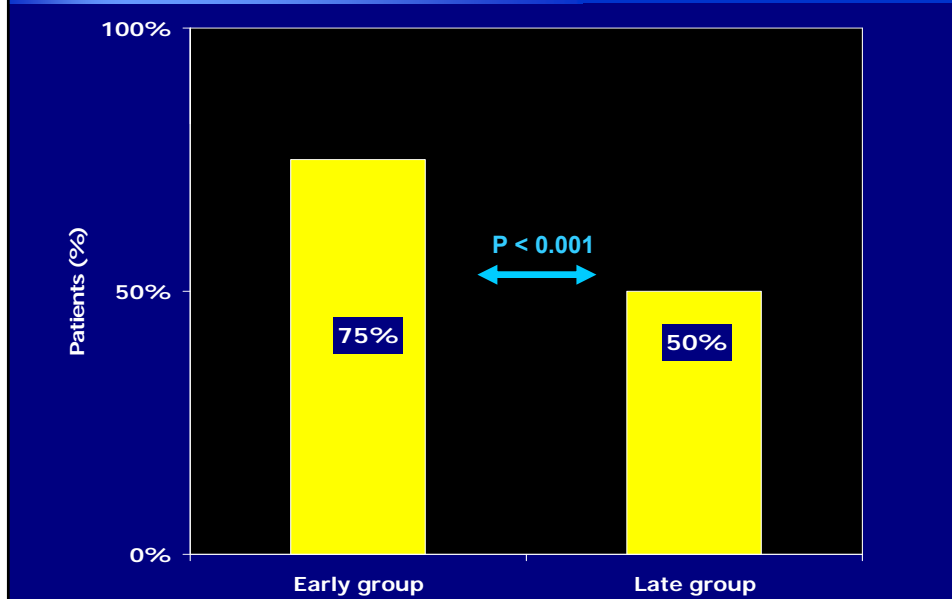
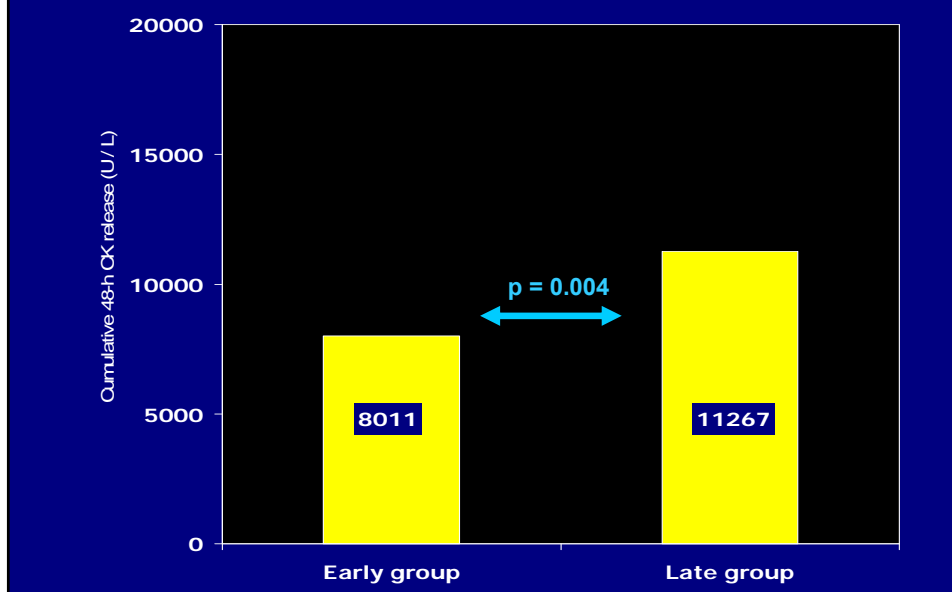
TREATMENT TIME INTERVALS



Interval measurement	Early group (n= 89)		Late group (n= 90)		<i>P</i>
	Median	IQR	Median	IQR	
Symptoms to balloon (min)	127	105- 178	165	118- 240	NS
Symptoms to abciximab (min)	63	44- 110	136	92- 207	0.001*
Start of abciximab to balloon (min)	61	48- 73	40	31- 54	0.001*

Angiographic and procedural results			
	Early group (n= 89)	Late group (n= 90)	P
Infarction related artery, n (%)			NS
Left main	1 (1)	1 (1)	
Left anterior descending	36 (40)	42 (47)	
Circumflex artery	11 (12)	12 (13)	
Right coronary artery	41 (46)	35 (39)	
Multivessel disease, n (%)			NS
2-vessel	26 (29)	23 (26)	
3-vessel	14 (16)	15 (17)	
Drug eluting stents, n (%)	48 (54)	40 (44)	NS
Number of stents	1.5 ±0.9	1.5 ±0.8	NS
Multiple stents, n (%)	31 (35)	33 (37)	NS



Secondary endpoints:**1) ST- segment deviation resolution $\geq 70\%$ at 90 min post-PCI****Secondary endpoints:****2) Enzymatic infarct size (by cumulative 48h CK release)**

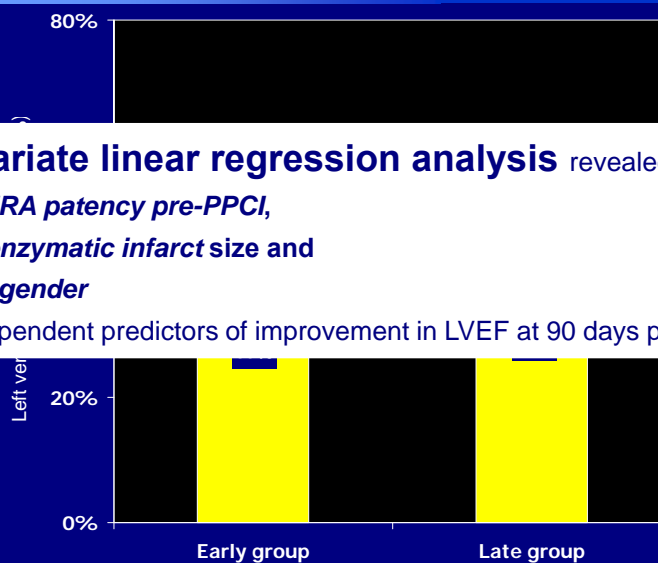
Secondary endpoints:

3) Three-month LV function results by gated SPECT

Multivariate linear regression analysis revealed that:

- Higher IRA patency pre-PPCI,
- Lower enzymatic infarct size and
- Female gender

were independent predictors of improvement in LVEF at 90 days post PPCI



Clinical outcome through follow-up (12 months)

	Early group (n= 89)	Late group (n= 90)	P
Cumulative MACE*, n (%)	8 (9)	21 (23)	0.009
Death, n (%)	2 (2)	4 (4)	NS
Recurrent MI, n (%)	2 (2)	6 (7)	NS
Revascularization, n (%)			NS
TVR	3 (3)	5 (6)	
TLR	1 (1)	3 (3)	
Non-TVTR	3 (3)	8 (9)	
Heart failure, n (%)	3 (3)	10 (11)	0.04
Major bleeding, n (%)	7 (8)	5 (6)	NS

* Cumulative MACE were calculated using only one (most serious event) per patient
death > recurrent MI > TVR or TLR > HF.

LIMITATIONS

Our study is a prospective, single-center but not randomized study.

However unfair comparison between the 2 groups is unlikely because of :

- 1) Comparable baseline patients characteristics,
 - 2) Low attrition rate,
 - 3) The physicians evaluating angiographic, ECG, laboratory, gated SPECT and clinical follow-up parameters were blinded to the assigned treatment,
 - 4) Fixed MISSION protocol through-out the study period.
- so it is unlikely that procedural changes over time other than the timing of abciximab administration have influenced the outcome.

Key findings of the study

In patients with STEMI treated with PPCI, early abciximab administration in the ambulance significantly improves:

pre-procedural IRA patency and
post-procedural ST-segment resolution,

Early abciximab therapy within the first 2 hours after symptoms onset (golden period) is associated with:

smaller infarct size,
improved LV function and
lower risk of heart failure



LEIDS UNIVERSITAIR MEDISCH CENTRUM

Thank you



PPCI thrombus is mostly a platelet rich thrombus

The aspirate, which was obtained with thrombosuction before angioplasty in patients with acute STEMI, contained platelet-rich thrombi in most patients,
Emphasizing the importance of early initiation of effective antiplatelet treatment in these patients.

*Svilaas et al. N Engl J Med 2008;
358: 557–67.*

Comparison between FINESSE, EUROTRANSFER & “EGYPT” cooperation meta-analysis			
RESULTS (early vs. late)	FINESSE Trial¹	EUROTRANSFER Registry²	“EGYPT” meta-analysis³
TIMI 2-3 flow pre-PCI	26% vs. 25%	34% vs. 21%*	23% vs. 13%*
ST segment resolution	33% vs. 31%	79% vs. 67%*	53% vs. 36%*
Enzymatic infarct size (CK)	1782 vs. 1860 U/L/hr	NA	WMD = - 111
LVEF assessment at 90 days follow-up	NA	NA	NA
Safety: Major bleeding	4.1 vs. 2.6%	2.3 vs. 1.4%	3.2 vs. 2.9%
Efficacy: MACE	<i>90 days</i>	<i>30 days</i>	<i>180 - 360days</i>
	10.7 vs. 10.5%	5.5 vs. 10.3%*	2.6% vs. 6.5%*

* = Significant ¹ FINESSE trial. N Engl J Med 2008; 358:2205-2217 ² EUROTRANSFER registry. Dudek et al. Presented ESC 2007 ³ De Luca et al. Heart online Jun 2008

Comparison between FINESSE, EUROTRANSFER & “EGYPT” cooperation meta-analysis			
Characteristics	FINESSE Trial¹	EUROTRANSFER Registry²	“EGYPT” meta-analysis³
Type	MC, RCT	MC, Registry	Individual pt. data
Sample size Early / Late abx.	806 / 818	727 / 359	840 / 822
Transferred patients	40%	100%	NA
PCI delay by protocol	> 60 – 240 min	No	No
Symptom to early abciximab {median}	165 min	120 min	100 min

* = Significant ¹ FINESSE trial. N Engl J Med 2008; 358:2205-2217 ² EUROTRANSFER registry. Dudek et al. Presented ESC 2007 ³ De Luca et al. Heart online Jun 2008

Discussion

-The subanalysis of the **ADMIRAL study**¹ showed that **early abciximab administration** improve clinical outcome as compared to late administration.

-Those studies with early abciximab administration **in the golden period** (first 2h after symptoms onset) appear to be those were the effect of the drug on the IRA patency, myocardial salvage and mortality is the most imperative.

- 1- **EGYPT cooperation metaanalysis**² -----100 min median Time
- 2- **Eurotrasfer registry**³ ----- 120 min median Time
- 3- **ON-TIME 2 RCT**⁴ ----- 76 min median Time
- 4- **Our study** ---- 63 min median Time

All these trials showed significant improvement in patency and on clinical outcomes.

on the other hand, the **FINESSE study** investigators recorded no benefit of early versus late administration of abciximab. **However, early abciximab was started fairly late (165 min) after the onset of symptoms.**

¹ ADMIRAL study.
N Engl J Med 2001;
344:1895-903.

² De luca et al. Heart online Jun 2008

³ EUROTRANSFER registry.
Dudek et al.
Presented ESC 2007

⁴ On – TIME 2 trial.
Lancet 2008;
372: 537–46

² FINESSE trial.
N Engl J Med 2008;
358:2205-2217