How to Mange STEMI in Very Elderly Patients

Jae Woong Choi MD. PhD.

Division of Cardiology

Eulji Hospital, Eulji University.

Definition of Elderly and Very Elderly
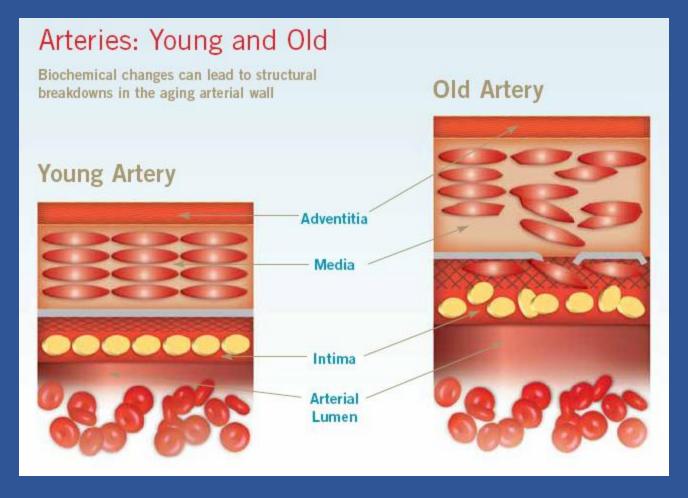
- No general definition
- UN cutoff is 60+
- Most developed countries have accepted the chronological age of

     65 as a 'elderly',

     75 as a 'very elderly'

     85+ as 'ultra elderly'

Age-related Changes in Vascular Integrity

Arteries: Young and Old

Biochemical changes can lead to structural breakdowns in the aging arterial wall

Young Artery

Old Artery

Adventitia

Media

Intima

Arterial Lumen

Effects of Aging on Coronary Arteries

- Dilation

- Tortuosity

- Media calcification

- Impaired endothelial function

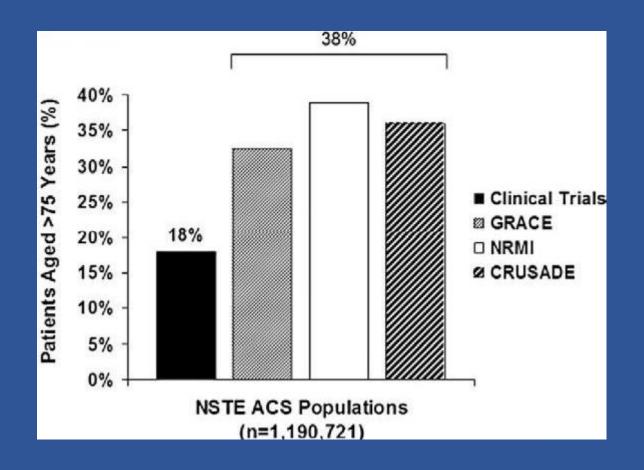# Factors Affecting Antiplatelet Efficacy and Safety in Very Elderly Patients with STEMI

Factors that may reduce efficacy

- Genetic polymorphisms
- Elevated clotting factor levels
- Increased aggregability
- Cellular dysfunction

Factors that may increase bleeding risk

- Elevated fibrinolytic protein
- Decreased vitamin K receptor
- Decreased renal clearance

Patients aged ≥75 years included in 5 VIGOUR clinical trials vs. 3 large community-based registries

Alexander et al. Am Heart J 2010
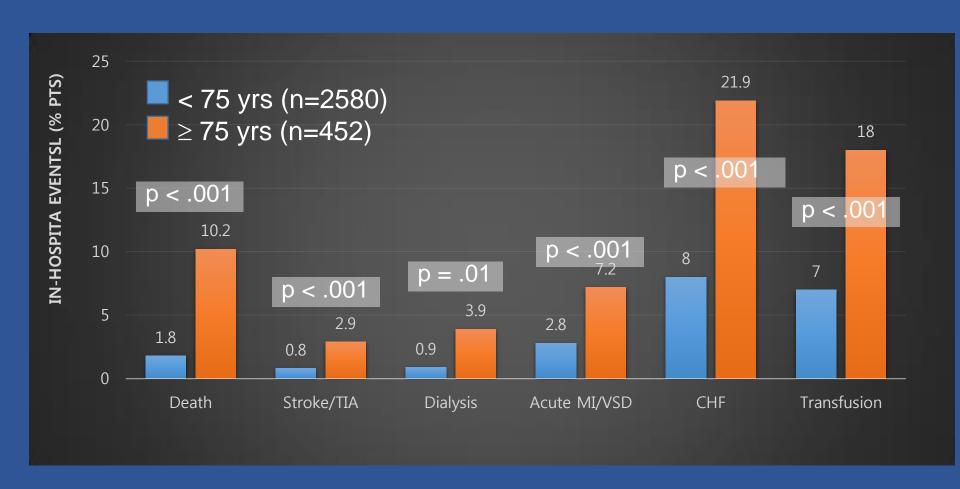
Reperfusion Therapy

Clinical and Angiographic Characteristics of Very Elderly Primary PCI (n=2262)

	<65 y (n = 1285)	65-74 y (n = 436)	75-84 y (n = 381)	P value
Male(%)	80.2	69.7	58.8	<.0001
BMI (kg/m2)	29.8 ± 6.0	28.3 ± 5.8	26.7 ± 4.6	<.0001
Cardiogenic shock	6.8	11.5	14.7	<.0001
Killip class ≥2	10	16.5	20.2	<.0001
Left main	0.3 (4)	1.6 (7)	1.6 (6)	<.001

Primary PCI in STEMI

	COR	LOE
Ischemic symptoms <12 h	I	A
Ischemic symptoms <12 h and contraindications to fibrinolytic therapy irrespective of time delay from FMC	I	B
Cardiogenic shock or acute severe HF irrespective of time delay from MI onset	I	B
Evidence of ongoing ischemia 12 to 24 h after symptom onset	IIa	B
PCI of a noninfarct artery at the time of primary PCI in patients without hemodynamic compromise	III: Harm	B

Complications after Primary PCI Based on Age

DeGeare and Grines AJC 2000;86:30

Primary Angioplasty vs. Fibrinolysis in Very Elderly Patients: Random Trial

de Boer (N=87) 2002

TRIANA (N=266) 2011

Senior PAMI (N=481) 2013

de Boer: A randomized comparison of primary angioplasty and thrombolytic therapy in elderly
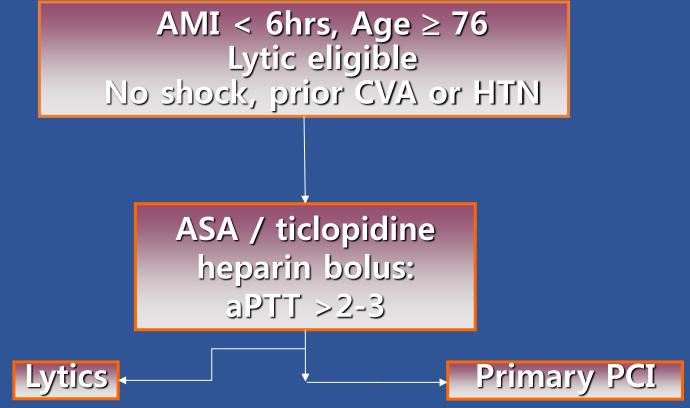
INCLUSION

- From March 1996 to April 1999
- 87 patients with an AMI who were older than 76 years
- AMI symptomes 30 min-6 hrs
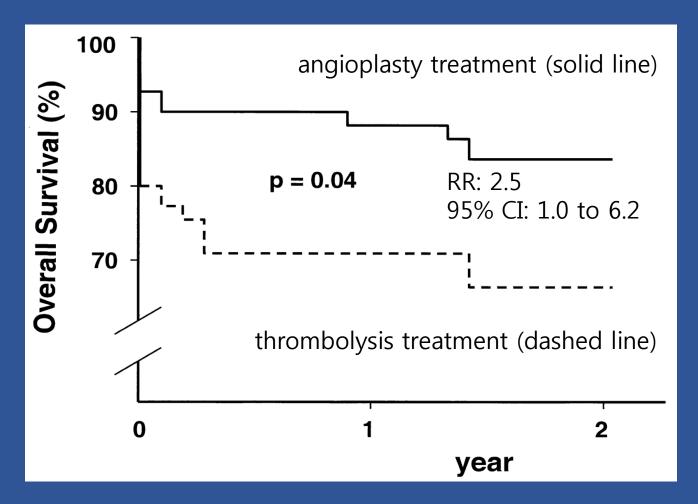- Between 6 h and 24h, if ischemia continue

EXCLUSION

- Cardiogenic shock
- Prior CVA, IC bleed or neoplasm
- BP > 180 systolic or > 100 diastolic

de Boer Study Algorithm

AMI < 6hrs, Age ≥ 76
Lytic eligible
No shock, prior CVA or HTN

ASA / ticlopidine
heparin bolus:
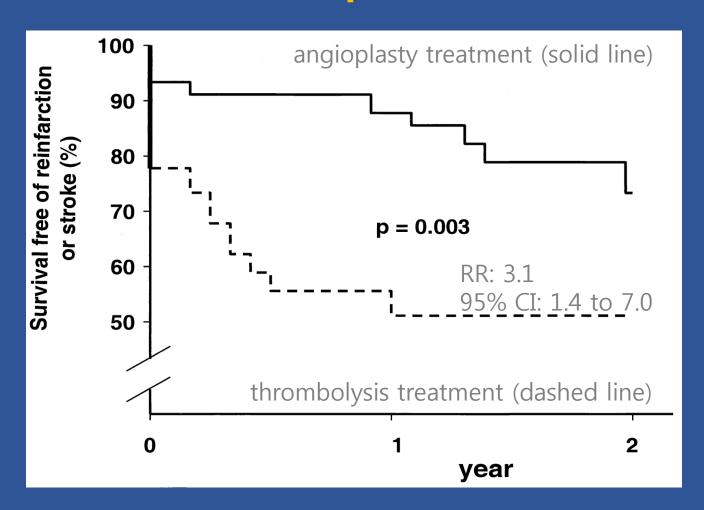aPTT >2-3

Lytics

Primary PCI

Primary Endpoint: Composite of death, reinfarction or stroke at 30 days
Secondary Endpoint: Composite of death, reinfarction or stroke at 1yrs

The Kaplan-Meier Curve Compares the Overall Survival for 24 ± 6 Months of Follow-up

angioplasty treatment (solid line)

p = 0.04

RR: 2.5
95% CI: 1.0 to 6.2

thrombolysis treatment (dashed line)

de Boer et al. JACC 39:11;1723. 2002

Overall Survival Free of Recurrent Infarction or Stroke for 24 ± 6 months of follow-up

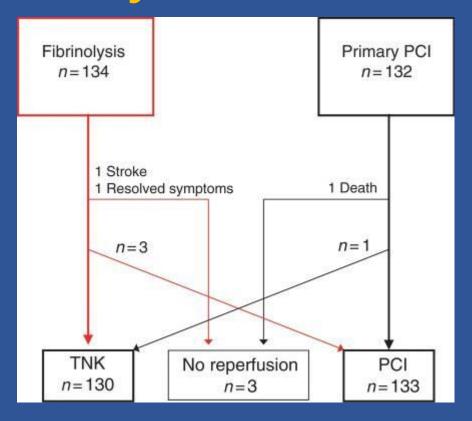de Boer et al. JACC 39:11;1723. 2002

TRIANA randomized trial

INCLUSION

- Aged ≥ 75 years. 166 patients.
- AMI symptoms 20 min – 6 hrs in duration
- ST elevation ≥ 1 mm or presumed new LBBB

EXCLUSION

- Contraindication to thrombolysis
- Cardiogenic shock
- STEMI caused by stent thrombosis
- CKD (creatinine >2.5mg/dL)

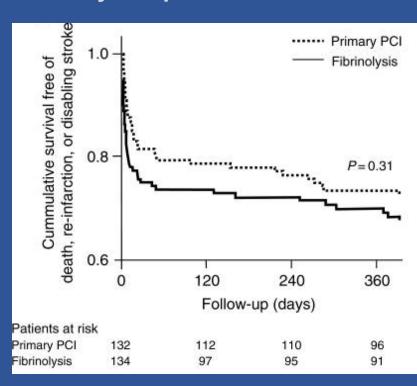# Chart flow of management in patients randomized to the TRIANA study

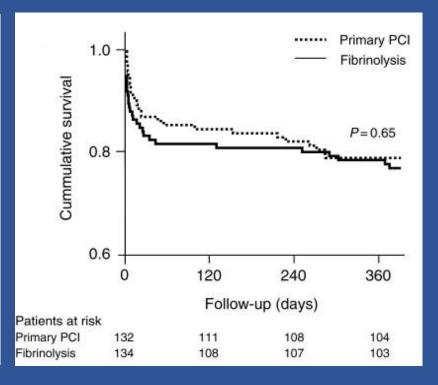Primary end point: Composite of all-cause mortality, re-infarction, or disabling stroke at 30 days.

Héctor Bueno et al.   Eur Heart J. 2011 Jan; 32(1): 51

One-year Kaplan–Meier survival curves free of death, re-infarction, or disabling stroke

Primary endpoint

All-cause mortality

Héctor Bueno et al.   Eur Heart J. 2011 Jan; 32(1): 51

Senior PAMI: A Multicenter International Randomized Trial Comparing Primary Angioplasty to Thrombolytic Therapy in the Elderly

Cindy L. Grines, M.D., F.A.C.C.

William Beaumont Hospital

Royal Oak, Michigan

Senior PAMI

- INCLUSION CRITERIA
  - 483 patients. Age ≥ 70 years
  - AMI symptoms 30 min – 12 hrs in duration
  - ST elevation ≥ 1 mm or presumed new LBBB
- EXCLUSION CRITERIA
  - Cardiogenic shock
  - Prior CVA, IC bleed or neoplasm
  - BP > 180 systolic or > 100 diastolic
  - Use of warfarin, INR > 1.4
  - Prolonged CPR, recent surgery or biopsy, active bleeding, etc.

Senior PAMI Study Algorithm

AMI < 12 hrs, Age ≥ 70
Lytic eligible
No shock, prior CVA or HTN

↓

ASA / clopidogrel/β blocker
60 U / kg heparin bolus

↓

Blocked randomization
Age 70-80, and Age > 80

Lytics ← → PCI + Abciximab

Primary Endpoint: 30-day death or disabling stroke
Secondary Endpoint: Death, disabling stoke or re-MI

Senior PAMI Stratified Randomization

N= 483 Randomized

Age 70-80
N=352

Age > 80
N=131

Lytics
N=168

PCI
N=184

Lytics
N=62

PCI
N=69
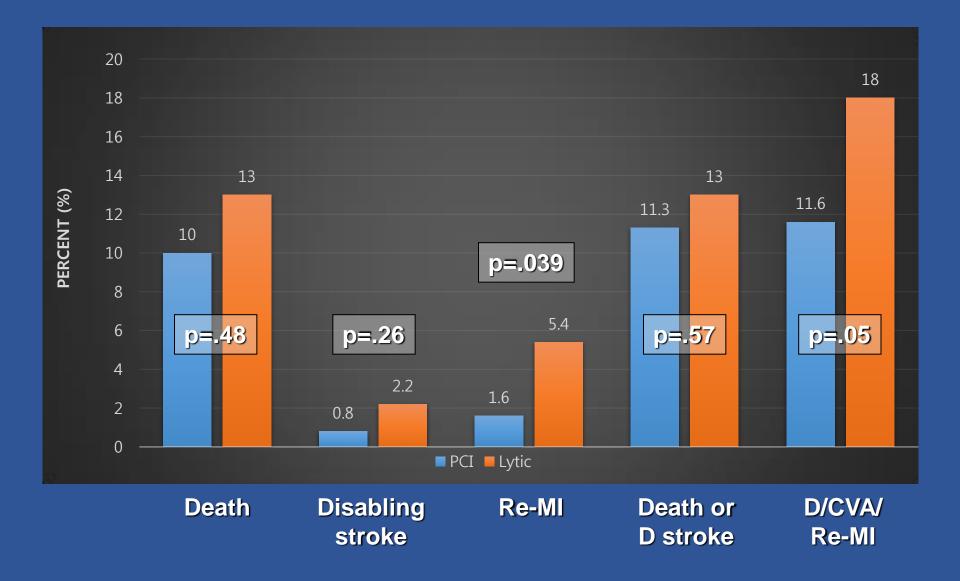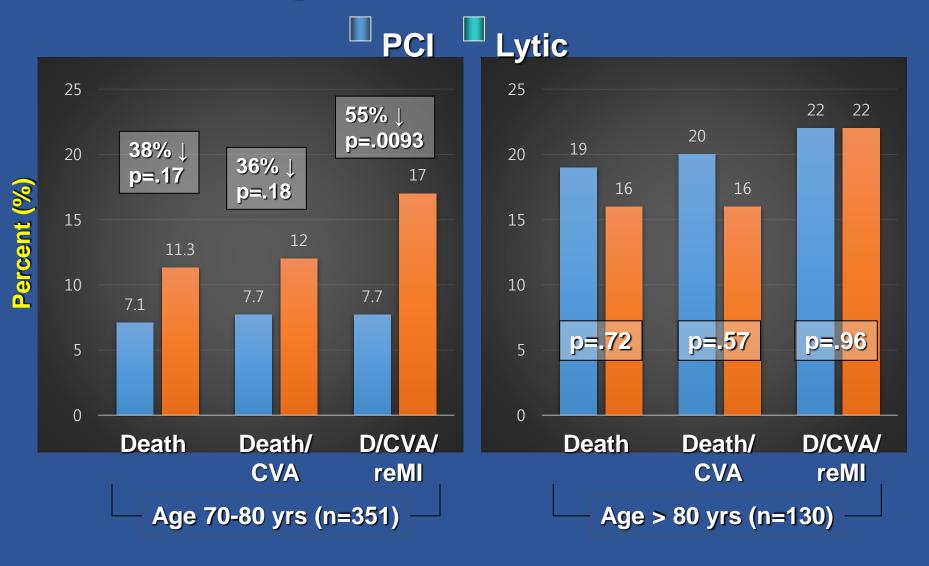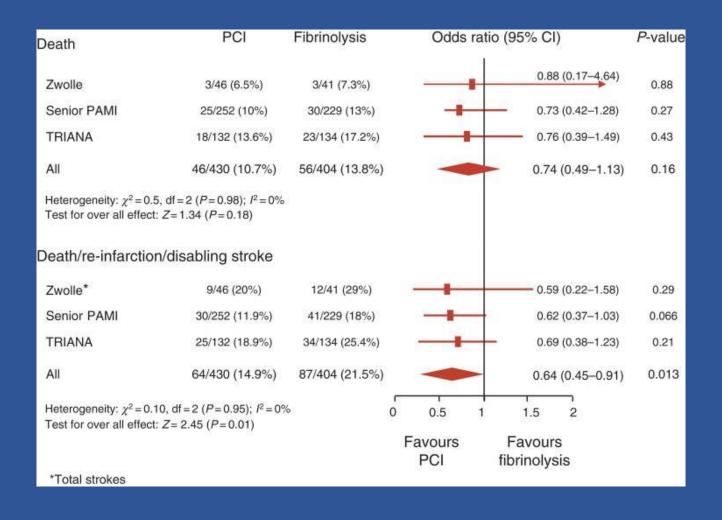
Senior PAMI: 30-Day Events

Senior PAMI: 30-Day Outcome Based on Age Stratified Randomization

Senior PAMI: Clinical Implications

- Primary PCI preferred reperfusion strategy in STEMI age ≤ 80 years

- In ultra-elderly patients (> 80 yrs) – primary PCI may not improve outcomes compared to thrombolytic therapy (however very small sample size N=130)

Meta-analysis of the Three Randomized Trials

Death	PCI	Fibrinolysis	Odds ratio (95% CI)	P-value
Zwolle	3/46 (6.5%)	3/41 (7.3%)	0.88 (0.17–4.64)	0.88
Senior PAMI	25/252 (10%)	30/229 (13%)	0.73 (0.42–1.28)	0.27
TRIANA	18/132 (13.6%)	23/134 (17.2%)	0.76 (0.39–1.49)	0.43
All	46/430 (10.7%)	56/404 (13.8%)	0.74 (0.49–1.13)	0.16

Heterogeneity: $\chi^2 = 0.5$, df = 2 ($P = 0.98$); $I^2 = 0\%$
Test for over all effect: $Z = 1.34$ ($P = 0.18$)

Death/re-infarction/disabling stroke	PCI	Fibrinolysis	Odds ratio (95% CI)	P-value
Zwolle*	9/46 (20%)	12/41 (29%)	0.59 (0.22–1.58)	0.29
Senior PAMI	30/252 (11.9%)	41/229 (18%)	0.62 (0.37–1.03)	0.066
TRIANA	25/132 (18.9%)	34/134 (25.4%)	0.69 (0.38–1.23)	0.21
All	64/430 (14.9%)	87/404 (21.5%)	0.64 (0.45–0.91)	0.013

Heterogeneity: $\chi^2 = 0.10$, df = 2 ($P = 0.95$); $I^2 = 0\%$
Test for over all effect: $Z = 2.45$ ($P = 0.01$)

Favours PCI   Favours fibrinolysis

*Total strokes

Cardiogenic Shock in Very Elderly

Early Revascularization of Cardiogenic Shock in Very Elderly
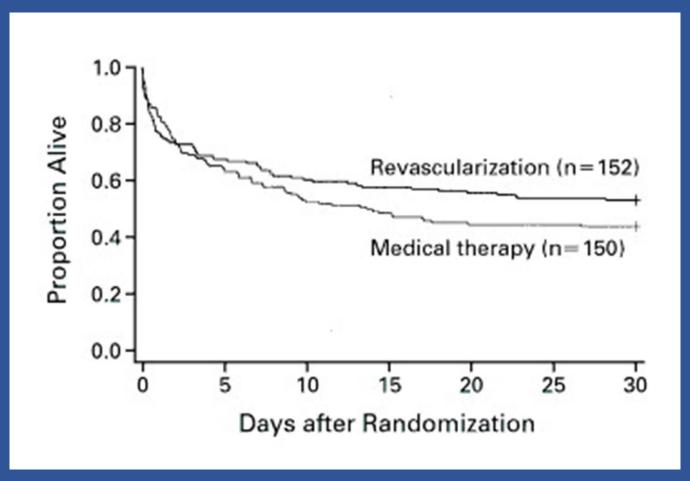
EARLY REVASCULARIZATION IN ACUTE MYOCARDIAL INFARCTION COMPLICATED BY CARDIOGENIC SHOCK
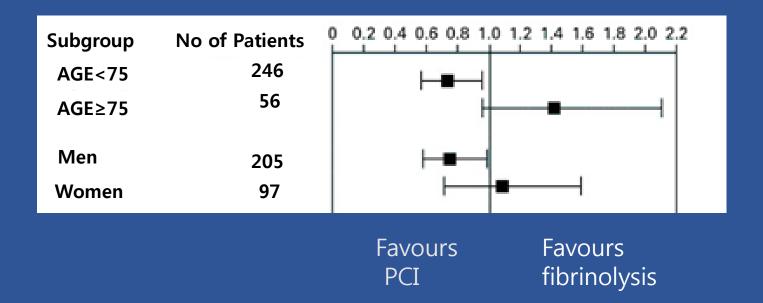
JUDITH S. HOCHMAN, M.D., LYNN A. SLEEPER, SC.D., JOHN G. WEBB, M.D., TIMOTHY A. SANBORN, M.D.,
HARVEY D. WHITE, D.SC., J. DAVID TALLEY, M.D., CHRISTOPHER E. BULLER, M.D., ALICE K. JACOBS, M.D.,
JAMES N. SLATER, M.D., JACQUES COL, M.D., SONJA M. MCKINLAY, PH.D., AND THIERRY H. LEJEMTEL, M.D.,
FOR THE SHOCK INVESTIGATORS*

Overall 30-Day Survival in the Study

Hochman JS et al. N Engl J Med 1999;341:625

30-Day Mortality According to Patient Subgroup

Subgroup	No of Patients
AGE<75	246
AGE≥75	56
Men	205
Women	97

Favours PCI — Favours fibrinolysis

Hochman JS et al. N Engl J Med 1999;341:625-634.

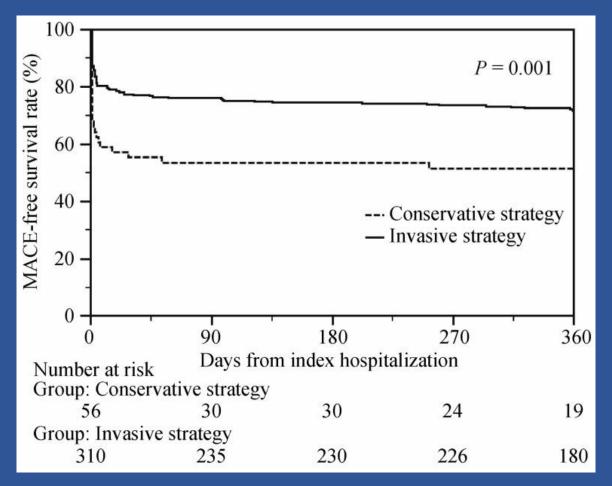# One-year Clinical Outcomes in Cardiogenic Shock in Elderly STEMI(KAMIR)

- From January 2008 to June 2011
- 13,473 patients were collected in the KAMIR.
- 1,565 elderly (aged ≥ 75 years) Cardiogenic shock patients

Baseline clinical characteristics.

	Conservative (n = 56)	Invasive (n = 310)	P value
Age (yrs)	80 ± 6	80 ± 6	0.929
Male	24 (42.9)	141 (45.5)	0.716
BMI (kg/m^2)	21.3 ± 3.7	22.3 ± 3.1	0.055
Risk Factor			
Hypertension	39 (69.6)	177 (57.0)	0.244
Previous MI	10 (17.9)	33 (10.6)	0.123
Diabetic mellitus	15 (26.7)	78 (25.1)	0.472
Physical findings			
Systolic BP (mmHg)	67 ± 20	67 ± 23	0.961
Heart rate	69 ± 46	60 ± 36	0.083
LVEF (%)	42 ± 16	45 ± 13	0.482

One-year Clinical Outcomes in acute STEMI Complicated by Cardiogenic Shock in Very Elderly Patients

One-year Kaplan-Meier estimates of MACE-free survival

Y.P Yoo. et al. J Geriatri Cardiol. 2013 Sep; 10(3): 235

Contrast Induced Nephropathy in Very Eldery

Contrast-Induced Nephropathy

Definition

- New onset or exacerbation of renal dysfunction after contrast administration in the absence of other causes:

increase by > 25%
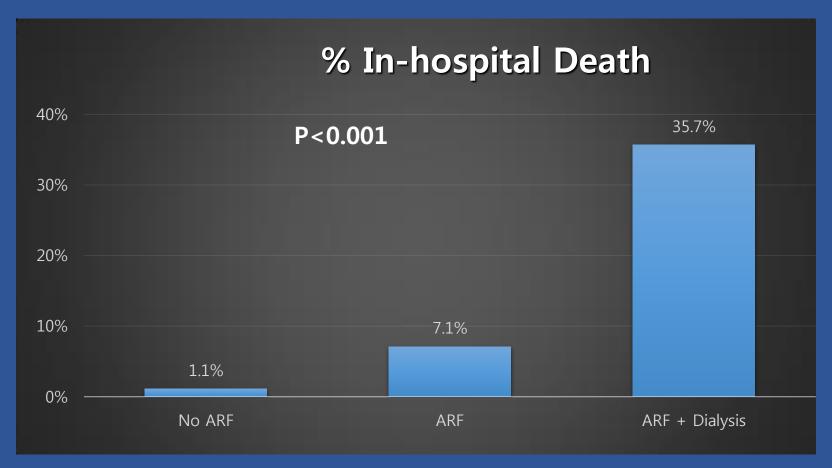
or

absolute ↑ of > 0.5 mg/dL

} **from baseline serum creatinine**

Occurs 24 to 48 hrs post–contrast exposure, with creatinine peaking 5 to 7 days later and normalizing within 7 to 10 days in most cases
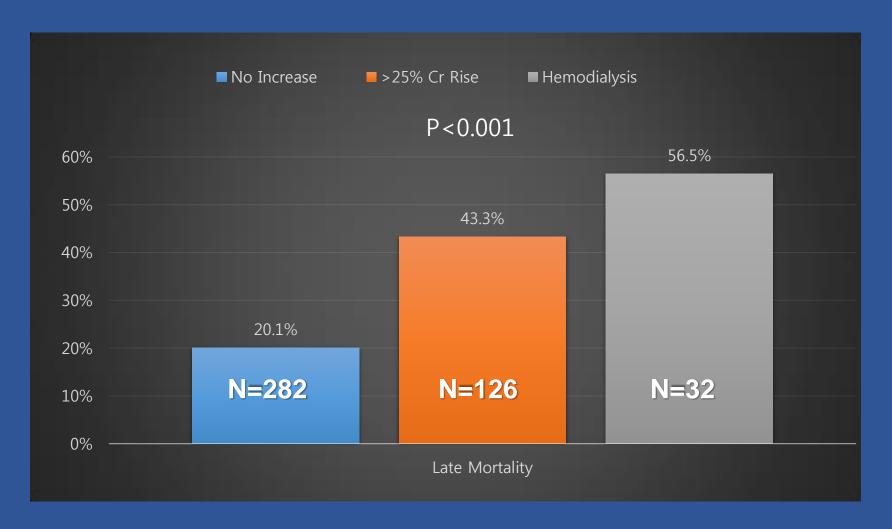
Predictor of CIN in patients undergoing primary PCI

	Odds Ratio	95% CI	P value
Age ≥ 75 years	4.8	1.08-2.94	< 0.042
Cardiogenic shock	8.8	2.61-9.74	< 0.01
GFR<60 mL/min/1.73m^2	10.3	2.71-15.76	< 0.01

Contrast-induced Nephropathy: In-hospital Mortality

% In-hospital Death

P<0.001

- No ARF: 1.1%
- ARF: 7.1%
- ARF + Dialysis: 35.7%

McCullough et al. Am J Med 1997;103:375

Late Mortality After PCI

McCullough et al. Am J Med 1997;103:375

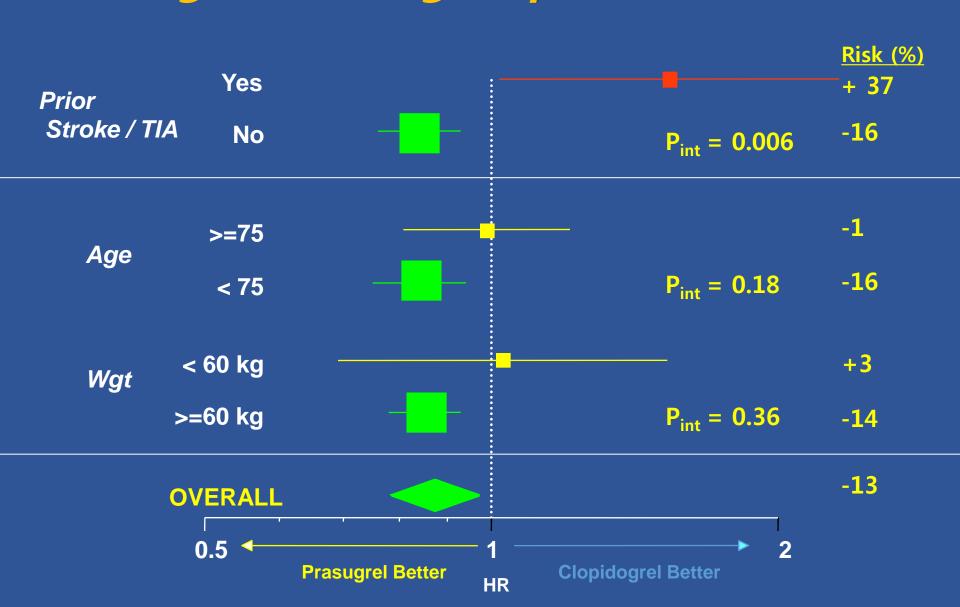# Prevention of CIN during primary PCI

- Low osmolar contrast agent

- Minimize contrast volume

- Avoid hypotension

- Maintain adequate hydration

- Avoid secondary contrast exposure (at least 72 hrs- ideally 2-3 weeks)

- Monitor renal function (24-72 hrs)

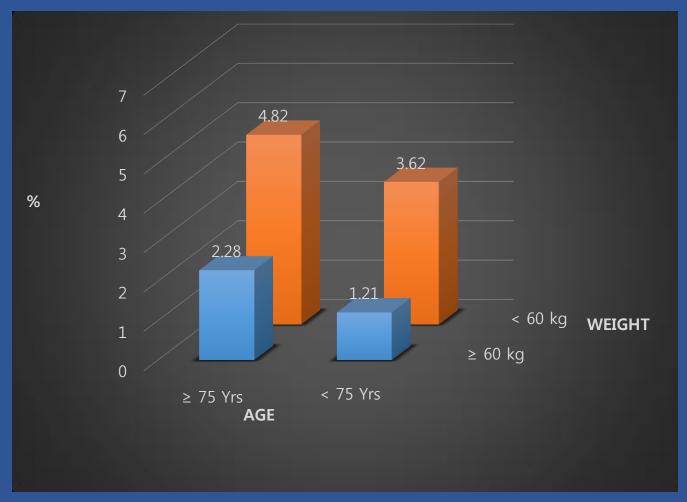# Antiplatelet Therapy to Support Primary PCI for STEMI

2012 ESC Guidelines on Periprocedural Oral Antiplatelet Therapy

Recommendations	Class[a]	Level[b]
Antiplatelet therapy		
Aspirin oral or i.v. (if unable to swallow) is recommended	I	B
An ADP-receptor blocker is recommended in addition to aspirin. Options are:	I	A
• Prasugrel in clopidogrel-naive patients, if no history of prior stroke/TIA, age <75 years.	I	B
• Ticagrelor.	I	B
• Clopidogrel, preferably when prasugrel or ticagrelor are either not available or contraindicated.	I	C

G Steg et al. European Heart Journal 2012

TRITON -TIMI-38: Net Clinical Benefit
Bleeding Risk Subgroups

Non-CABG TIMI Major Bleeding (After 3 days) for Prasugrel Group Impact of Weight and Age
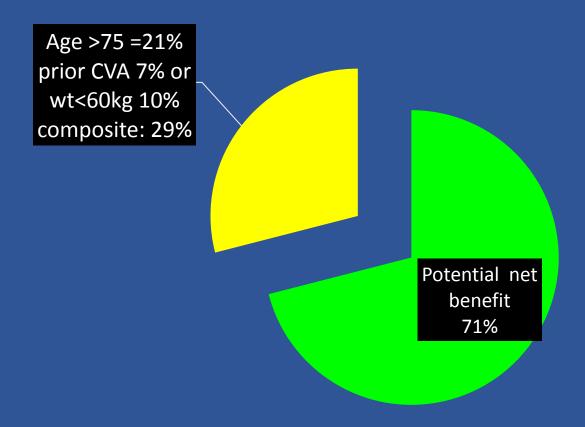

FDA Advisory Board Presentation, Washington DC Feb 2009

Ticagreor vs. Clopidogrel in Very Eldery Sub-analysis From the PLATO

	Ticagrelor	Clopidogrel	HR (95% CI)	Interaction p-value
CV death, MI or stroke				
> 75 years	17.2	18.3	0.94 (0.78 - 1.13)	0.22
< 75 years	8.6	10.4	0.82 (0.74 - 0.91)	
Total death				
> 75 years	9.8	12.4	0.81 (0.65 - 1.03)	0.78
< 75 years	3.6	4.8	0.78 (0.67 - 0.92)	
Definite stent thrombosis				
> 75 years	1.8	2.1	0.66 (0.30 - 1.45)	0.94
< 75 years	1.3	1.9	0.67 (0.49 - 0.93)	
Major bleeding				
> 75 years	14.2	13.5	1.04 (0.84 - 1.28)	1.00
< 75 years	11.2	10.8	1.04 (0.94 - 1.15)	
Non-CABG major bleed.				
> 75 years	8.3	7.1	1.16 (0.87 - 1.55)	0.78
< 75 years	3.9	3.2	1.22 (1.02 - 1.46)	

Pts at Risk of Bleeding In a Real World Setting

Age >75 =21% prior CVA 7% or wt<60kg 10% composite: 29%

Potential net benefit 71%

OHI STEMI database n=2069

Summary

- Very elderly patients with STEMI should not be managed just based on their age differently from younger patients.

- The lack of substantial evidence make clinical decision often very difficulty.

Summary

- Age related pharmacokinetic change and potential pro and cones of primary PCI should be considered.

Management of the Very Elderly Patient with STEMI

- Over utilization of medications (Bleeding, CIN)

- Lower rates of revascularization

- Higher complication rates with invasive procedures