How to Manage 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 \( \geq 75 \) 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)

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

DeGeare and Grines  AJC 2000;86:30
### Primary PCI in STEMI

<table>
<thead>
<tr>
<th>Condition</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic symptoms &lt; 12 h</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Ischemic symptoms &lt; 12 h and contraindications to fibrinolytic therapy irrespective of time delay from FMC</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Cardiogenic shock or acute severe HF irrespective of time delay from MI onset</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Evidence of ongoing ischemia 12 to 24 h after symptom onset</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>PCI of a noninfarct artery at the time of primary PCI in patients without hemodynamic compromise</td>
<td>III: Harm</td>
<td>B</td>
</tr>
</tbody>
</table>
Complications after Primary PCI Based on Age

<table>
<thead>
<tr>
<th></th>
<th>&lt; 75 yrs (n=2580)</th>
<th>≥ 75 yrs (n=452)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>1.8</td>
<td>10.2</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>0.8</td>
<td>2.9</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Dialysis</td>
<td>0.9</td>
<td>3.9</td>
<td>.01</td>
</tr>
<tr>
<td>Acute MI/VSD</td>
<td>2.8</td>
<td>7.2</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>CHF</td>
<td>8</td>
<td>21.9</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Transfusion</td>
<td>7</td>
<td>18</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

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 symptoms 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 et al. JACC 39:11;1723. 2002*
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)

thrombolysis treatment (dashed line)

p = 0.04

RR: 2.5
95% CI: 1.0 to 6.2

de Boer et al. JACC 39:11;1723. 2002
Overall Survival Free of Recurrent Infarction or Stroke for $24 \pm 6$ months of follow-up

angioplasty treatment (solid line)

thrombolysis treatment (dashed line)

$\text{RR: } 3.1$
$95\% \text{ CI: } 1.4 \text{ to } 7.0$

$p = 0.003$

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.

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

Primary endpoint

All-cause mortality

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 stroke or re-MI
Senior PAMI Stratified Randomization

N= 483 Randomized

Age 70-80
N=352

Lytics
N=168
PCI
N=184

Age > 80
N=131

Lytics
N=62
PCI
N=69
Senior PAMI: 30-Day Events

<table>
<thead>
<tr>
<th>Event</th>
<th>PCI</th>
<th>Lytic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>10</td>
<td>13</td>
<td>0.48</td>
</tr>
<tr>
<td>Disabling stroke</td>
<td>0.8</td>
<td>2.2</td>
<td>0.26</td>
</tr>
<tr>
<td>Re-MI</td>
<td>1.6</td>
<td>5.4</td>
<td>0.039</td>
</tr>
<tr>
<td>Death or D stroke</td>
<td>11.3</td>
<td>13</td>
<td>0.57</td>
</tr>
<tr>
<td>D/CVA/Re-MI</td>
<td>11.6</td>
<td>18</td>
<td>0.05</td>
</tr>
</tbody>
</table>
Senior PAMI: 30-Day Outcome Based on Age Stratified Randomization

Based on Age Stratified Randomization

Death

Age 70-80 yrs (n=351)

PCI

Lytic

Death

Death/CVA

D/CVA/reMI

Age > 80 yrs (n=130)

Percent (%)

38% ↓

p=.17

36% ↓

p=.18

55% ↓

p=.0093

p=.72

p=.57

p=.96
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

<table>
<thead>
<tr>
<th>Death</th>
<th>PCI</th>
<th>Fibrinolysis</th>
<th>Odds ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zwolle</td>
<td>3/46 (6.5%)</td>
<td>3/41 (7.3%)</td>
<td>0.88 (0.17–4.64)</td>
<td>0.68</td>
</tr>
<tr>
<td>Senior PAMI</td>
<td>25/252 (10%)</td>
<td>30/229 (13%)</td>
<td>0.73 (0.42–1.28)</td>
<td>0.27</td>
</tr>
<tr>
<td>TRIANA</td>
<td>18/132 (13.6%)</td>
<td>23/134 (17.2%)</td>
<td>0.76 (0.39–1.49)</td>
<td>0.43</td>
</tr>
<tr>
<td>All</td>
<td>46/430 (10.7%)</td>
<td>56/404 (13.8%)</td>
<td>0.74 (0.49–1.13)</td>
<td>0.16</td>
</tr>
</tbody>
</table>

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

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

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

*Total strokes
Cardiogenic Shock in Very Elderly
Early Revascularization of Cardiogenic Shock in Very Elderly

The New England Journal of Medicine

© Copyright, 1999, by the Massachusetts Medical Society

VOLUME 341 AUGUST 26, 1999 NUMBER 9

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*

* Correspondence to: Dr. Timothy A. Sanborn, Massachusetts General Hospital, Charlestown, MA 02129.
Overall 30-Day Survival in the Study

30-Day Mortality According to Patient Subgroup

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>No of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE&lt;75</td>
<td>246</td>
</tr>
<tr>
<td>AGE≥75</td>
<td>56</td>
</tr>
<tr>
<td>Men</td>
<td>205</td>
</tr>
<tr>
<td>Women</td>
<td>97</td>
</tr>
</tbody>
</table>

Favours PCI

Favours fibrinolysis

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

Yeon Pyo Yoo, Myung Ho Jeong and Korean Acute Myocardial Infarction Registry Investigators. J Geriatr Cardiol V 10(3); 2013
## Baseline clinical characteristics.

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

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 75 years</td>
<td>4.8</td>
<td>1.08-2.94</td>
<td>&lt; 0.042</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>8.8</td>
<td>2.61-9.74</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>GFR&lt;60 mL/min/1.73m²</td>
<td>10.3</td>
<td>2.71-15.76</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

Fabrice Ivanes et al. Archives of Cardiovascular Diseases 107;8: 424
Contrast-induced Nephropathy: In-hospital Mortality

% In-hospital Death

P < 0.001

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

Late Mortality After PCI

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

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

*G Steg et al. European Heart Journal 2012*
TRITON -TIMI-38: Net Clinical Benefit

Bleeding Risk Subgroups

Prior Stroke / TIA
- Yes
- No

Age
- >=75
- < 75

Wgt
- < 60 kg
- >=60 kg

OVERALL

Comparison of Prasugrel vs. Clopidogrel

- Prasugrel Better
- Clopidogrel Better

Risk (%)
- +37
- -16
- -1
- -16
- +3
- -14
- -13

P_{int} values:
- P_{int} = 0.006
- P_{int} = 0.18
- P_{int} = 0.36

Adjusted HR values:
- 0.5
- 1
- 2
Non-CABG TIMI Major Bleeding (After 3 days) for Prasugrel Group Impact of Weight and Age

FDA Advisory Board Presentation, Washington DC Feb 2009
### Ticagrelor vs. Clopidogrel in Very Elderly Sub-analysis From the PLATO

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

*Husted S et al. J Am Coll Cardiol. 2011;57:E1009*
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 difficult.
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