Cardiovascular disease is the most frequent diagnosis in elderly people and is the leading cause of death in both men and women older than 65 years. Every year in the United States more than 700,000 patients arrive at the emergency room with ST-segment elevation myocardial infarction (STEMI). About 60 percent of hospital admissions for AMI are of people older than 65 years. Their in-hospital, 1-month, and 1-year mortality is high. In this article, we will provide a review on clinical trials that guide the management of STEMI myocardial infarction of the elderly patients.

**Management strategies for patients with STEMI**

With the advent of thrombolytic therapy and primary coronary interventions (PCI), there came a great opportunity to open acutely occluded infarct-related artery (IRA) and restore antegrade flow to the ischemic myocardium. The strategies which guide the cardiologist from the first encounter with the patient in the emergency room through the discharge day and the office follow-up are listed in table 1.

**Table 1. Management strategies for patients with STEMI**

1. Quickly screen patients for indications and risks of reperfusion therapy
2. Start thrombolytic therapy or send the patient quickly to the cardiac catheterization laboratories for emergency angioplasty and stenting
3. Open the infarct-related artery and its distal microvasculature with minimal incidence of stroke (<1%) by the fastest (<90 minutes; door to balloon time) and most effective way (<3% 30-day mortality, <4% reinfarction, <2% restenosis in 1 year)
4. Prevent left ventricular (LV) remodeling (no LV dilation)
5. Prevent another MI in the future (secondary prevention)

From the angiographic point of view, successful reperfusion is defined as early and complete restoration of coronary blood flow to a Thrombolysis In acute Myocardial Infarction (TIMI) 3 flow. This brisk flow allows sufficient microvascular perfusion to result in significant reduction in mortality.

**Thrombolytic therapy**

The indications for thrombolytic therapy are for patients presenting with chest discomfort within 12 hours of onset and with ST-segment elevation (1 mm in at least 2 limb leads and 2 mm in 2 or more contiguous precordial leads suggestive of STEMI) or new left bundle branch block. The advantage of thrombolytic therapy is by earliest restoration of flow due to its quick and simple intravenous administration. It does not restore full epicardial or microvascular flow to the majority of patients, nor sustain its patency thereafter. The results of thrombolytic therapy for the elderly patients were shown in the SENIOR PAMI trial where thrombolytic therapy and PCI was compared in present environment with betablocker (BB), angiotensin converting enzyme inhibitor (ACEI), clopidogrel, aspirin (ASA), glycoprotein 2b3a inhibitors (GPI) and drug-eluting stent (DES) etc.

The SENIOR PAMI trial

In the SENIOR-PAMI, a multicenter, randomized trial comparing primary PCI to thrombolytic therapy, 483 patients aged 70 and above were randomized for primary PCI or thrombolytic therapy. At 30-day, for patients aged from 70-80, the mortality rate was 7% for PCI and 11% for thrombolytic therapy. The rate of stroke was 1.2% to 2.2%, intra-cranial hemorrhage (ICH) was 0% vs. 1.3%, respectively. So the conclusions showed that PCI was superior to thrombolytic therapy at reducing combined endpoints of death, disabling stroke, and reinfarction but not the pre-established endpoints of death or disabling stroke. The advantage of PCI is to avoid ICH and reduce reinfarction and recurrent ischemia. The results only benefits the 70-80 years of age. 2
The results in very old patients (>80) showed no difference in mortality (19% vs 16%), mortality + cardiovascular accident (CVA) + reinfarction (both 22%) between thrombolytic therapy and PCI. However, from the statistical point of view, the >80 years old group had a small sample size (n=130). These results confirmed the same findings of prior trial in Japan.

**Thrombolytic therapy and PCI in patients >80 years of age**

A hundred and twenty patients aged 80 years and older at relatively low risk with AMI were randomized into a primary PTCA group (n = 61) or a "conservative" no-PTCA group (n = 59). Long-term follow-up showed that the LV EF, the end-diastolic volume index and end-systolic volume index were significantly increased and similar in both groups at 6 months after AMI. With endpoints of all causes of death, cardiac death, reinfarction, congestive heart failure (CHF), and CVA, a 3-year Kaplan-Meier event-free survival rate analysis revealed no significant benefits in the PTCA group. The authors concluded that primary PTCA for very elderly patients with AMI appears to have few beneficial effects on combined events during a 3-year period. Second, early PTCA did not prevent LV remodeling after AMI in patients at relatively low risk.25

**Strokes and bleeding after thrombolytic therapy for the elderly patients**

Thrombolytic therapy is associated with an increase in stroke risk (3 to 8 additional strokes per 1000 treated patients), especially ICH which happened more in elderly patients of more than 75 years of age.2 In the Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO)-I trial, ICH occurred more frequently in patients receiving alteplase compared to streptokinase, in particular patients over the age of 75. The results were duplicated again in the GUSTO-III trial, in which there was a trend of ICH increase with reteplase in patients aged over 75. However, in the Fibrinolytic Therapy Trialists' meta-analysis6 old age was not an independently predictive factor for excess bleeding. This could be due to selection bias because elderly patients with increased risk for ICH might not have been enrolled.

**Primary coronary intervention**

With DES because of the incomplete results of thrombolytic therapy and inelegibility of many patients with it, balloon angioplasty (POBA) and PCI was performed on patients with STEMI. Bare metal stent (BMS) was deployed in order to improve the angiographic achievements of POBA and sustain its long term clinical results. With the development of DES and its track record of low in-stent-restenosis for elective stenting, DES was tried in STEMI patients with hope for long term patency. The safety, short and long term efficacy of DES in STEMI patients was tested in the randomized clinical trial (RCT) below.

**Drug eluting stent for STEMI: the TYPHOON trial**

Seven hundred and twelve patients with STEMI randomized between Cypher stents and balloon angioplasty plus BMS. The results showed that at 1 year, the rate of mortality was 2.2% for both groups. The overall rate of target vessel failure was 7.3% for the Cypher stent and 14.3% among those treated with balloon angioplasty and a BMS (a 49% relative reduction). In a substudy with 210 patients, there was 83% reduction in the rate of restenosis and an 83% reduction in tissue proliferation. The stent thrombosis rate was 3.4% for DES and 3.6% for POBA or BMS. These results met the expectations of low mortality and excellent long term major adverse cardiovascular events (MACE).4

However, the results of PCI in STEMI are operator dependent and institution related. The indicators of excellent interventional service of a cardiac catheterization laboratory are listed in Table 2. If these results are suboptimal than the national level, then the focus of treatment for patients with STEMI in that particular hospital should be the use of thrombolytic therapy, with further referral to PCI when indicated.5 Patients with STEMI should be referred for primary PCI once the cardiac catheterization laboratories provide better services which are translated into better patient outcomes.

<table>
<thead>
<tr>
<th>Table 2. Indicators of excellence in providing interventional service for STEMI</th>
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<tr>
<td>1. Door to balloon time &lt;90 minutes</td>
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<td>2. TIMI 2 or 3 flow attained in &gt;90% of patients</td>
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<tr>
<td>3. Emergency CAGB &lt;2%</td>
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<td>4. Actual performance of PCI in &gt;85% brought to the laboratory</td>
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<tr>
<td>5. Risk-adjusted in-hospital mortality rate 3% in patients without cardiogenic shock</td>
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**Stroke and bleeding in the elderly patients undergoing PCI after thrombolytic therapy**

However, if the elderly patients cannot undergo PCI on time, they could receive thrombolytic therapy. When it is logistically feasible, then they could undergo PCI. What is the risk of ICH and bleeding after thrombolytic therapy followed by PCI?

**The ASSENT-4 PCI trial** In the ASSENT-4 trial, thrombolytic agent TNK was given at full dose to STEMI patients who were being referred for primary PCI. The results showed that mortality, recurrent MI, stroke, ICH and major bleeding, as well as stent thrombosis, were all significantly increased in patients who had received full-dose thrombolytic therapy prior to primary PCI. The overall 30-day mortality was quite low, just 3.8% for primary PCI and quite high, 6.0% for the thrombolytic therapy + PCI patients.6

**Thrombolytic therapy or transfer for PCI: options for the elderly patients**

The technical success rate of stenting after STEMI has been remarkably high while the procedural complication rate
was extremely low, even when more high risk patients were included. In the large NIMR 2-3 registry of more than 300,000 patients, the result of PCI was excellent if performed by experienced operators, in high volume interventional laboratories while there was no difference in mortality between thrombolytic therapy or mechanical interventions in low-volume hospitals. As more patients with STEMI prefer mechanical interventions, the problem now is the availability of this modality of treatment. Only 20% of US hospitals have cardiac catheterization laboratories and even less have the capability of performing emergency PCI. Although transfer of the MI patient to a facility that can perform PCI is possible, 87% of transferred patients had more than 2 hours delay which may theoretically outweigh any added benefit. In the case of PCI to be done in hospitals without on-site surgical capability, the results from the Atlantic Cardiovascular Patient Outcomes Research Project trial of primary PCI versus thrombolysis in STEMI (C-PORT) trials showed that the transferred patients had better outcome than the patients who received locally thrombolytic therapy. An excellent mortality result is dependent on short door-to-balloon time, optimally less than 90 minutes, which is not attainable in every US cardiac catheterization laboratory.

**Was long door-to-balloon time detrimental for the elderly patients?**

A total of 2,322 consecutive patients treated with primary PCI were prospectively identified and followed up for a median of 83 months. The results showed that prolonged door-to-balloon times (0 to 1.4 h vs 1.5 to 1.9 h vs 2.0 to 2.9 h vs ≥ 3.0 h) were associated with higher in-hospital mortality (4.9% vs 6.1% vs 8.0% vs 12.2%, P < 0.0001) and late mortality (12.6% vs 16.4% vs 20.4% vs 27.1% at 7 years, P < 0.0001) and were an independent predictor of late mortality by Cox regression (P = 0.0004). Prolonged door-to-balloon times (≥2 h vs < 2 h) were associated with higher late mortality in high-risk patients (32.5% vs 21.5%; P = 0.0002) but not in low-risk patients (10.8% vs 9.2%; P = 0.53) and in patients presenting early (3 h) (24.7% vs 15.0%; P = 0.0001) but not in late presentation (>3 h) (21.1% vs 18.5%; P = 0.80).  

**Who are the high risk patients?**

The patients who need expedited process for PCI are the ones with high risks and with short interval from symptom onset to presentation. The high risk patients are the patients with anterior wall MI, with Killip more than class 2, and older than 65 years of age. The interventional cardiologists can make a difference in mortality of these high risk patients (including the elderly patients) by focusing and making a real effort to shorten the door-to-balloon time. While the patients with low risk and long interval between symptom onset to presentation also need to have a short door to balloon time, they do not benefit from an expedited PCI (from a statistical point of view) because the window of myocardial salvage is passed or the MI is too small to be benefited from invasive interventions. These understandings are to rationalize the fairness in triage and to give priority to patient who should go for PCI first, or be transferred first when 2 patients arrive at the same time, in the same emergency room or are transferred from different hospitals.

**Adjunctive medications**

**Acetylsalicylic Acid**

Aspirin (ASA) is a weak platelet inhibitor; it works by irreversibly acetylating cyclooxygenase. ASA suppresses the production of the pro-aggregatory arachidonic-acid-mediated effect of thromboxane A2. Data from the second International Study of Infarct Survival (ISIS-2), which included 3,411 patients over 70 years of age, confirmed that ASA was at least as efficacious in older as in younger patients.

**Thienopyridine**

Clopidogrel is a thienopyridine derivative that inhibits the binding of adenosine diphosphate to its platelet receptors. It begins to exert its effectiveness 24 hours after a loading dose of 300-600mg when >80% of platelets are inhibited. It has been effective in preventing the formation of thrombus after elective stenting for stable angina and improves outcomes in patients with acute coronary syndrome (ACS). The efficacy of thienopyridine in STEMI was tested in the CLARITY-TIMI 28 trial. There was no trial for the elderly patient per se.

**The CLARITY-TIMI 28 trial**

The Clopidogrel as Adjunctive Reperfusion Therapy-TIMI 28 trial enrolled 3,493 patients with STEMI and randomized them to receive either clopidogrel (300-mg loading dose, then 75 mg once daily) or placebo. Of these patients, 53.4% underwent PCI and received open-label clopidogrel. The results demonstrated that pretreatment with clopidogrel resulted in a highly significant reduction in cardiovascular death, MI, or stroke from randomization through 30 days (7.5% vs 12.0%). There was no significant excess in the rates of TIMI major or minor bleeding (2.0% vs 1.9%) between clopidogrel- and placebo-treatment groups.

**Glycoprotein 2b3a inhibition in the elderly patients**

The platelet glycoprotein 2b3a receptor mediates the final pathway of platelet aggregation. This receptor becomes activated by a variety of soluble and adhesive agonists, and binds fibrinogen molecules between platelets in the aggregation process. The linkage of these fibrins provides a strong network to trap red cells, and subsequently form a firm thrombus. The GP 2b3a inhibitors (GPI) inhibit the cross-linking of platelets by fibrinogen, thus effectively prevent formation of newer clot.

**Combination of thrombolytic therapy and glycoprotein 2b3a inhibition in the elderly patients**

Because of the effectiveness of GPI on platelet aggregation on patients going for PCI, GPI was given to patients with AMI in an attempt to improve the TIMI 3 flow and possibly the mortality.

**The GUSTO V trial**

The Global Utilization of Strategies to Open Occluded Coronary Arteries-V (GUSTO V) study randomized 16,588 patients (average age, 61; 2,237 patients
with age > 75 years) to reteplase with and without abciximab. Patients > 75 years of age had twice the number of ICH than those less than 75 years of age (P = 0.006). At 1-year follow-up, no additional survival benefit was seen in the thrombolytic therapy + GPI arm over the thrombolytic therapy arm in the elderly subgroup. So another PCI and GPI trial (CADDILLAC) was designed to examine the impact of age after primary PCI and to determine whether routine coronary stent implantation and/or platelet GPI improve the clinical outcomes in elderly patients.

The CADDILLAC trial 2,082 patients with AMI were randomized to balloon angioplasty, angioplasty plus abciximab, stenting alone, or stenting plus abciximab. No patient was excluded on the basis of advanced age; patients ranging from 21 to 95 years of age were enrolled. One-year mortality increased for each decile of age, exponentially after 65 years of age (1.6% for patients < 55 years, 2.1% for 55 to 65 years, 7.1% for 65 to 75 years, 11.1% for patients > 75 years; P < 0.0001). Elderly patients also had increased rates of stroke and major bleeding compared with their younger counterparts. Among elderly patients (≥ 65 years), 1-year rates of ischemic target revascularization (7.0% vs 17.6%; P < 0.0001) and subacute or late thrombosis (0% vs 2.2%; P = 0.005) were reduced with stenting compared with balloon angioplasty.

Routine abciximab administration, although safe, was not of definite benefit in elderly patients. Rates of mortality, reinfarction, disabling stroke, and major bleeding in the elderly were independent of reperfusion modality. Despite contemporary mechanical reperfusion strategies, mortality, major bleeding, and stroke rates remain high in elderly patients undergoing primary PCI, outcomes that are not affected by stents or GPI. By reducing restenosis, however, stent implantation improves clinical outcomes in elderly patients with AMI.

Unfractionated heparin

Unfractionated heparin (UFH) is used to prevent the propagation of the thrombus, formation of new mural thrombosis, systemic embolism, and coronary reoclusion. It also prevents the formation of a stable fibrin clot by inhibiting the activation of the fibrin stabilizing factor. It is indicated when the STEMI patients receive relatively fibrin-specific agents, such as alteplase or reteplase, which produce a variable effect on the systemic coagulation system, and in many patients very little breakdown of fibrinogen or depletion of coagulation factors. The thrombolytic therapy is maintained at 1.5-2 times control (50-70 seconds).

In patients undergoing primary interventions, UFH is not continued after the procedure because it has not been proven to decrease the rate of reocclusion or ischemia.

Low molecular weight heparin (LMWH)

LMWH is smaller fraction of UFH and has a more predictable anticoagulant effect. Routine laboratory monitoring is not required. The efficacy of LMWH was tested in the ASSENT-3 plus trial, in which 1,639 patients with STEMI were randomly assigned to treatment with tenecteplase and either 1) intravenous bolus of 30 mg enoxaparin followed by 1 mg/kg subcutaneously BID for a maximum of 7 days or 2) weight-adjusted UFH for 48 hours. The results showed that enoxaparin tended to reduce the composite of 30-day mortality or in-hospital reinfarction, or in-hospital refractory ischemia to 14.2% vs 17.4% for UFH (P = 0.080). However, there were increases in total stroke (2.9% vs 1.3%, P = 0.026) and intracranial hemorrhage (2.20% vs 0.97%, P = 0.047) seen in patients > 75 years of age. Since then, a new trial testing LMWH in STEMI is being conducted. As part of this new trial, reduced doses of enoxaparin were given to the elderly patient to determine whether a more carefully defined dose of enoxaparin can maintain the thrombolytic results while avoiding the excess bleeding.

The EXTRACT-TIMI 25 trial

In the Enoxaparin and Thrombolysis Reperfusion for Acute Myocardial Infarction-Study TIMI 25 trial, 20,506 patients with STEMI who were scheduled to undergo fibrinolysis received enoxaparin throughout the index hospitalization or UFH for at least 48 hours. At 30 days, the results showed that the primary efficacy end point (death or nonfatal recurrent MI) occurred in 12% of patients in the UFH group and 9.9% of those in the enoxaparin group (17% reduction in relative risk, P < 0.001). Nonfatal reinfarction occurred in 4.5% of the patients receiving UFH and 3% of those receiving enoxaparin (33% reduction in relative risk, P < 0.001); 7.5% of patients given UFH died, as did 6.9% of those given enoxaparin (P = 0.11). The composite of death, nonfatal reinfarction, or urgent revascularization occurred in 14.5% of patients given UFH and 11.7% of those given enoxaparin (P < 0.001); major bleeding occurred in 1.4% and 2.1%, respectively (P < 0.001). The composite of death, nonfatal reinfarction, or nonfatal ICH (a measure of net clinical benefit) occurred in 12.2% of patients given UFH and 10.1% of those given enoxaparin (P < 0.001).

Thrombolytic therapy and LMWH and GP and PCI

In the Assessment of the Safety and Efficacy of a New Thrombolytic Regimen-3 (ASSENT-3) trial 6,095 patients (average age, 61; 13% with age > 75 years) with a STEMI were randomized to receive full-dose tenecteplase plus enoxaparin, half-dose tenecteplase plus abciximab plus unfractionated heparin, or full-dose tenecteplase plus unfractionated heparin. The primary efficacy combined end point (death at 30 days, in-hospital reinfarction, and refractory ischemia) revealed that tenecteplase plus enoxaparin was better than tenecteplase plus unfractionated heparin. The use of abciximab with thrombolytic therapy showed no benefit in patients > 75 years old, in contrary to clear benefits observed in those < 75 years old. ICH or major bleeding happened more in patients older than 75 years of age.

Direct thrombin inhibitor

In a meta-analysis of patients with STEMI in the Direct Thrombin Inhibitor Trialists' collaboration, direct thrombin inhibitor (DTI) was found to reduce the rate of reinfarction at
30 days (3.9% vs 4.8% with UFH, \( P < 0.001 \)), but did not reduce mortality (9.1% vs 9.0%, \( P=0.68 \)) or the combined incidence of death/reinfarction at 30 days (11.8% vs 12.4, \( P=0.18 \)).\(^{23} \) DTI was not given for STEMI.

**Beta-blockers**

Systemic review of RCTs of beta-blockers (BB) in STEMI has found that BB given within hours of infarction reduced both mortality and reinfarction. BB may reduce the rates of cardiac rupture and ventricular fibrillation. This may explain why people older than 65 years of age and those with large infarcts benefit the most, as they also have higher rate of complications. In patients with moderate HF (NYHA class II or III), BB were found to decrease readmission, mortality and sudden death.\(^{24} \) The benefits of BB was evidenced in patients with STEMI after thrombolytic therapy or before PCI.

However, in the CADILLAC trial, BB was beneficial to the patients who were not on prior BB therapy.\(^{25} \) Although these trials were conducted in the pre-reperfusion era, the results remain applicable today, since the majority of older MI patients are not managed with a reperfusion strategy. Lower dosages of BB may be appropriate in patients over 75 years of age.

**Angiotensin converting enzyme inhibitors (ACEI)**

The elderly constitute an increasing proportion of AMI patients and have disproportionately high mortality and morbidity. Those with HF or impaired LV function after AMI have high complication and mortality rates. The benefits of counteracting the mechanism of dilatory LV remodeling by inhibition of the angiotensin converting enzyme (ACE) are well evidenced in many trials of patients with chronic HF. Data from the third Italian Group Study (GISSI-3),\(^{26} \) which included 5,124 patients over the age of 70, indicate that although early treatment with oral lisinopril has no effect on total mortality, it is associated with a modest but statistically significant 17% reduction in the composite outcome of death, HF, or severe LV dysfunction in older patients. The latest results of ACEI in patients with AMI and LV dysfunction was proved in the PREAMI study below.

**Perindopril and Remodeling in Elderly with Acute Myocardial Infarction (PREAMI),** a double-blind, randomized, parallel-group, multicenter, placebo-controlled study, determined whether similar benefits occur in elderly postinfarction patients with preserved LV function. A total of 1,252 patients 65 years or older with a LV ejection fraction of 40% or higher and recent AMI were randomized to receive perindopril erbumine or placebo (8 mg/d) for 12 months. The combined primary end point was death, hospitalization for HF, or LV remodeling. Secondary end points included cardiovascular death, hospitalization for reinfarction or angina, and revascularization.\(^{27} \)

The results showed that the primary end point occurred in 181 patients (35%) taking perindopril and 290 patients (57%) taking placebo, with a significant absolute risk reduction of 0.22 (95% confidence interval, 0.16 to 0.28; \( P<0.001 \)). A total of 126 patients (28%) and 226 patients (51%) in the perindopril and placebo groups, respectively, experienced remodeling. The mean increase in LV end-diastolic volume was 0.7 mL with perindopril compared with 4.0 mL with placebo (\( P<0.001 \)). In the perindopril group, 40 deaths (6%) and 22 hospitalizations (4%) for HF occurred, whereas 37 deaths (6%) and 30 hospitalizations (5%) occurred in the placebo group. Treatment did not affect death, whereas the hospitalization rate for HF was slightly reduced (absolute risk reduction, 0.01; 95% confidence interval, -0.01 to 0.02). No treatment effect on other secondary end points was detected.\(^{27} \)

The 1-year treatment with 8 mg/d of perindopril reduces progressive LV remodeling that can occur even in the presence of small infarct size, but it was not associated with better clinical outcomes. These results were similar to the ones of GISSI-3 study.

**Angiotensin II receptor blockers in the elderly patients**

Angiotensin receptor blocker (ARB) is a new blocker acting on the angiotensin receptor. It was tried on patients with CHF. In the Losartan Heart Failure Survival Study (ELITE) II trial,\(^{25} \) the results showed that losartan caused fewer side effects than captopril, but losartan was not superior in reducing morbidity and mortality. In order to clarify these beneficial effects, ARBs were compared with ACEI in patients with STEMI complicated by LV dysfunction especially in the elderly patients.

**The Valsartan in Acute Myocardial Infarction Trial (VALIANT)** randomized 14,703 patients with HF and/or LV ejection fraction <40% to receive captopril, valsartan, or both. Mortality and a composite end point, including cardiovascular mortality, readmission for HF, reinfarction, stroke, and resuscitated cardiac arrest, were compared for the age groups of <65 (n=6998), 65 to 74 (n=4,555), 75 to 84 (n=2,777), and > or =85 (n=383) years. With increasing age, 3-year mortality almost quadrupled (13.4%, 26.3%, 36.0%, and 52.1%, respectively), composite end-point events more than doubled (25.2%, 41.0%, 52.3%, and 66.8%), and hospital admissions for HF almost tripled (12.0%, 23.1%, 31.3%, and 35.4%). Outcomes did not differ between the 3 study treatments in any age group. Adverse events associated with captopril and valsartan were more common in the elderly and in patients receiving combination therapy. With increasing age, use of aspirin, beta-blockers, and statins declined, and use of digoxin, calcium-channel blockers, and non-potassium-sparing diuretics increased. On 3-year multivariable analysis, each 10-year age increase was associated with a hazard ratio of 1.49 (95% CI, 1.426 to 1.557; \( P<0.001 \)) for mortality and an odds ratio of 1.38 (95% CI, 1.31 to 1.46; \( P<0.001 \)) for readmission with HF. The outcomes remained poor in elderly patients with HF and/or impaired LV systolic function after AMI, although most received beta-blockers and all received an ACE inhibitor and/or an angiotensin receptor blocker.\(^{29} \)

The above data reflect the equality of ARBs and ACEI administration to patients with MI and congestive HF. This is
of particular importance in individuals who are ACEI-intolerant. The combination of ARB and ACEI was not superior to either class alone when given shortly after acute MI complicated by CHF. Better therapies and increased use of aspirin, beta-blockers, and statins are needed in this important and increasing patient group.  

Lipid lowering drugs
Statin therapy is known to decrease mortality in patients with stable angina, ACS or prior MI. RCTs with statin were conducted in order to clarify the benefits of statins on patients in the acute phase of STEMI. However, it is unclear whether statins exert a similar effect in reducing the incidence of recurrent AMI and death when used in the elderly patients.

Statin in elderly patients with AMI A retrospective cohort study (1997-2002) to compare 5 statins using data from medical administrative databases in 3 provinces (Quebec, Ontario and British Columbia) was conducted. Patients aged 65 years and over who were discharged alive after their first AMI-related hospital stay and who began statin treatment within 90 days after discharge were included. The primary end point was the combined outcome of recurrent AMI or death from any cause. The secondary end point was death from any cause. Adjusted hazard ratios (HRs) for each statin compared with atorvastatin as the reference drug were estimated using Cox proportional hazards regression analysis. A total of 18,637 patients were included. The results showed that statins were effective for secondary prevention in elderly patients after AMI.  

Complication and concomitant conditions in elderly patients with STEMI

Cardiogenic shock
SHOCK trial In the SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial, patients over the age of 75 years, with AMI and cardiogenic shock (CS), had higher 30-day and 6-month mortality rates after revascularization than with medical therapy (relative risk [RR], 1.41; \( P = 0.01 \)).  

This finding is particularly disturbing, since patients over 75 account for more than one half of all cases of CS. However, in the patients screened for the SHOCK trial and not enrolled (the SHOCK trial Registry), these patients showed different results with early or late mechanical revascularization.

The SHOCK trial Registry In the SHOCK Trial Registry with shock due to pump failure aged <75 years (n=588) and \( \geq 75 \) years (n=277), and 30-day mortality of patients treated with early revascularization <18 hours since onset of shock were compared with those undergoing a later or no revascularization procedure. After excluding early deaths covariate-adjusted relative risk and 95% confidence intervals were calculated to compare the revascularization strategies within the two age groups. Older patients more often had prior MI, CHF, renal insufficiency, other comorbidities, and severe coronary anatomy. In-hospital mortality in the early vs. late or no revascularization groups was 45 vs 61% for patients aged <75 years (\( P = 0.002 \)) and 48 vs 81% for those aged \( \geq 75 \) years (\( P = 0.0003 \)). After exclusion of 65 early deaths and covariate adjustment, the relative risk was 0.76 (0.59, 0.99; \( P = 0.045 \)) in patients aged <75 years and 0.46 (0.28, 0.75; \( P = 0.002 \)) in patients aged \( \geq 75 \) years.  

The elderly patients with MI complicated by cardiogenic shock are less likely to be treated with invasive therapies than younger patients with shock. Covariate-adjusted modeling reveals that elderly patients selected for early revascularization have a lower mortality rate than those receiving a revascularization procedure later or never.

Cardiogenic shock in the real world The applicability of this subset analysis from a select patient population enrolled in a randomized trial to the general population is unclear. At the Mayo Clinic between 1991 and 2000, the outcome of all patients \( \geq 75 \) years old with CS caused by MI who underwent urgent PCI was evaluated. The study included 61 patients with a mean age of 79.5±3 years; 21% of these patients had a history of prior coronary artery bypass grafting (CABG), 41% had had a prior MI, 28% had diabetes mellitus, and 18% had a history of a CVA. PCI was performed 8.0±7.2 hours after onset of MI. Angiographic success (<50% residual stenosis) was achieved in 91% of the lesions that were dilated. In hospital outcomes included death (44%), CABG (1.6%), and CVA (4.9%). The 30-day mortality rate was 47%. The estimated survival rate 1 year after discharge (Kaplan Meier method) was 75%.  

These results confirm a high early mortality rate among patients \( \geq 75 \) years old with MI complicated by CS, but suggest that among patients referred for angiography, outcomes may be better than previously believed when early revascularization is performed. In this population, 56% of patients survived to be discharged from the hospital, and of the hospital survivors, 75% were alive at 1 year.

Anemia in the elderly patients
Anemia may have adverse effects in patients with coronary artery disease. However, the benefit of blood transfusion in elderly patients with AMI and various degrees of anemia is uncertain.

Retrospective Medicare data on anemia A retrospective study of data on 78,974 Medicare beneficiaries 65 years old or older who were hospitalized with AMI was conducted. Patients were categorized according to the hematocrit on admission (5.0 to 24.0%, 24.1 to 27.0%, 27.1 to 30.0%, 30.1 to 33.0%, 33.1 to 36.0%, 36.1 to 39.0%, or 39.1 to 48.0%), and data were evaluated to determine whether there was an association between the use of transfusion and 30-day mortality. The results showed that the patients with lower hematocrit values on admission had higher 30-day mortality rates. Blood transfusion was associated with a reduction in 30-day mortality among patients whose hematocrit on admission fell into the categories ranging from 5.0% to 24.0% (adjusted odds ratio, 0.22; 95% confidence interval, 0.11 to 0.45) to 30.1% to 33.0% (adjusted odds ratio, 0.69; 95% confidence interval, 0.53 to 0.89). It was not associated with a reduction in 30-day mortality among those whose hematocrit values fell in the
higher ranges. In one of seven subgroup analyses (among patients who survived at least two days), transfusion was not associated with a reduction in mortality for patients with hematocrit values of 30.1% or higher. So in the care of elderly patients, physicians must recognize that age per se does not cause positive or negative outcomes, but rather that it is a marker for underlying pathophysiologic factors and comorbid illnesses that may influence treatment effects. For the patients above 80 years, neither thrombolytic therapy nor PCI help them to live longer. Thrombolytic therapy caused more ICH. Other management includes BB, full antiplatelet drug coverage, ACEI and cholesterol lowering drug, complete revascularization, treatment of anemia and high glucose level, bleeding prevention at the arterial access site and in the gastro-intestinal tract (due to antiplatelet drug). Attention to details and meticulous treatment could influence the outcomes of the elderly patients with AMI.

Blood transfusion is associated with a lower short-term mortality rate among elderly patients with AMI if the hematocrit on admission is 30.0% or lower and may be effective in patients with a hematocrit as high as 33.0% on admission.

High glucose level in the elderly patients

The relationship between admission glucose levels and outcomes in older diabetic and nondiabetic patients with AMI is not well defined.

Glucose level in the elderly patients with AMI

A national sample of elderly patients (n=141,680) hospitalized with AMI from 1994 to 1996 were evaluated. Admission glucose was analyzed as a categorical (<110, >110 to 140, >140 to 170, >170 to 240, >240 mg/dl) and continuous variable for its association with mortality in patients with and without recognized diabetes. The results showed that a substantial proportion of hyperglycemic patients (eg, 26% of those with glucose >240 mg/dl) did not have recognized diabetes. Fewer hyperglycemic patients without known diabetes received insulin during hospitalization than diabetics with similar glucose levels (eg, glucose >240 mg/dl, 22% vs 73%; P<0.001). Higher glucose levels were associated with greater risk of 30-day mortality in patients without known diabetes (for glucose range from <110 to >240 mg/dl, 10% to 39%) compared with diabetics (range, 16% to 24%; P for interaction <0.001). After multivariable adjustment, higher glucose levels continued to be associated with a graded increase in 30-day mortality in patients without known diabetes (for glucose range from <110 to >240 mg/dl, HR, 1.87; 95% CI, 1.75 to 2.00). In contrast, among diabetic patients, greater mortality risk was observed only in those with glucose >240 mg/dl (HR, 1.32; 95% CI, 1.17 to 1.50 versus glucose <110 mg/dl; P for interaction <0.001). One-year mortality results were similar. So elevated glucose is common, rarely treated, and associated with increased mortality risk in the elderly patients with AMI, particularly those without recognized diabetes.

Conclusions

Based on worldwide availability of facilities, logistics, and resources affordability, especially in developing countries, the benchmark reperfusion strategy remains thrombolytic therapy. However, given the availability of catheterization laboratories, interventional expertise, rapid restoration of patency by catheter-based reperfusion can result in excellent outcomes. This is certainly the case in institutions with large volume interventional laboratories and experienced operators. However, even PCI was beneficial to the young patients, the >75 years of age elderly patients did not benefit from mortality except reduction of stroke and re-infarction.

References

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