



## Effect of Captopril and Age factor among Chinese Cardiovascular patients

Tabish Hussain<sup>1</sup> MBBS, MD, Li Yu Shu<sup>1</sup> MD, PhD, Cheng Xiang<sup>1</sup> MD, PhD, Tumenjavkhlan Sosorburam<sup>2</sup> MD

1. Department of Internal Medicine and Cardiology, Union Hospital, Tongji Medical College, Huazhong University of Sciences and Technology, Wuhan, 430030, China

2. Department of Anesthesia, Tongji Hospital, Tongji Medical College, Huazhong University of Sciences and Technology, Wuhan, 430030, China

### RESEARCH

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#### Corresponding Author:

Tabish Hussain

Room No .403, International Doctors Building, Tongji Medical College, Huazhong University of Sciences and Technology, Wuhan, 430030, China  
[drtabish@hotmail.com](mailto:drtabish@hotmail.com)

### Abstract

#### Background

Since, ACE inhibitors (Angiotensin Converting enzyme inhibitors) like Captopril have reportedly shown a cardiac beneficial role after coronary event but there is no such study which has ruled out its efficacy among different age groups. So this study aim was to rule out the effect of aging and efficacy of Captopril among Chinese cardiovascular patients with acute myocardial infarction (MI) during the hospitalization phase of therapy.

#### Method

Randomized study was conducted at Tongji Medical College Hospital with recruitment of 100 Chinese patients, mean age  $64 \pm 10$  years with 53% males. All presented with first time acute MI and received standard conventional therapy, including intravenous-thrombolysis, oral aspirin with beta blocker. Later, they were randomly divided to Captopril-STUDY group and Conventional therapy-CONTROL group and were further subdivided in 4 groups depending on age. Statistical analyses were done to formulate the correlation between multi-variables.

#### Results

Systolic blood pressure in 60 patients receiving Captopril was significantly lower than in 40 patients who got the conventional therapy only ( $135.6 \pm 14.4$  mmHg/ $82.8 \pm 10.3$  mmHg vs.  $144.1 \pm 18.8$  mmHg/ $83.2 \pm 11.3$  mmHg,  $P < 0.05$ ). Overall 4 patients in the study group and 9 patients in control group died within the hospital (6.67% vs. 22.5%,  $P < 0.0001$ ). Careful data analysis proved that the survival of patients on Captopril correlated significantly with age ( $P < 0.001$ ). Patient's survival was statistically significant with respect to age ( $P < 0.001$ ). Survival rate was better among elderly on Captopril in comparison to younger ones during the hospitalization. Other significant multivariates were smoking, ejection fraction beta-blocker use, cardiac enzyme levels and the intravenous thrombolysis.

#### Conclusion

Survival with Captopril is more in elderly Chinese patients than young reflecting that ACE-inhibitors in proper dosage play a real beneficial role among elderly after acute MI.

#### Key Words

Acute Myocardial Infarction, Aging, Angiotensin-Converting Enzyme Inhibitor

### Background

Right after the myocardial infarction, the neuro-endocrine system gets activated. Left ventricle dilatation is linked to increase in size of infarcted zone as expansion and the remodelling of the ventricle<sup>1, 2</sup>. Long-term ACE inhibitor therapy usually improve the outcome of cardiovascular disease specially acute myocardial infarction by altering the mechanism of infarct expansion and left ventricular remodelling which may result in left ventricular dilatation and activation of the neuro-endocrine system<sup>3,4,5 and 6</sup>. Treatment of cardiac failure patients with ACE inhibitors accompanied by acute ischemic event leads to an improvement in prognosis<sup>7</sup>, with additional benefits of



limited adverse ventricular remodelling and reduced incidence of recurrent infarction<sup>8, 9</sup>. ACE inhibitor therapy among patients of myocardial infarction has survival benefits as well. Primary mechanism has been proved to alter the change in volume of the left ventricle and by improving its performance during systole<sup>3, 7 and 10</sup>.

Captopril can remarkably improve the diastolic filling so as to decrease the left ventricular load after myocardial infarction<sup>11</sup>. It also limit the decline in function of adjacent non-infarcted areas which is an important determinant of LV remodeling<sup>12</sup>. Captopril causes acute selective enhancement of LV relaxation without disturbing the coronary blood flow, possibly through an endogenous bradykinin and nitric oxide neuro-endocrine pathway<sup>13</sup> thus exhibiting many beneficial effects. Cardiac rehabilitation phase is the key in determining the future prospects, and making a probability about upcoming cardiac problems and among patients with acute myocardial infarction, it is usually divided primarily to hospitalization phase (phase 1-inpatient) and follow-up phase (phase 2 and 3 Phase 2 - Outpatient Programme (from hospital discharge to 12 weeks) .Phase 3 - Maintenance Programme (ongoing, to maintain health gains, cardiac club) of rehabilitation lasting usually up to 6 months from the day of infarction<sup>14</sup>. Among patients with first time myocardial infarction event, age may be a powerful independent indicator of mortality rate within the hospital, age-related increase in the mortality rate cannot be explained by large infarcts<sup>15, 16 and 17</sup>.

Efficacy of Ace inhibitors has already been proven among patients of acute myocardial infarction, but there is very little data available regarding its efficacy among various age groups and during different phases of cardiac rehabilitation<sup>18</sup> as most of conclusions about the effects of ACE-Inhibitors have been drawn from animal models on ischemic events of the heart on acute basis<sup>1, 7, 8 and 9</sup>. So, the aim of this study was to evaluate the clinical efficacy of ACE inhibitors in various age group cardiovascular patients after acute myocardial infarction with primary focus of its benefits during the hospitalization phase of early rehabilitation.

## Method

This randomized study was conducted at Union Hospital, Tongji Medical College allied tertiary care teaching hospital, Wuhan, China for a period of six months from April 2009 to September 2009. A total of 100 patients were recruited in the study. Mean age was 64 ±10 years. 53 were males. All patients suffered first time acute myocardial infarction and

were hospitalized within 72 hours of symptoms. After admission, they received standard conventional therapy for acute myocardial infarction, including intravenous thrombolysis and oral aspirin or beta blocker metoprolol. Then they were randomly allocated to either the **Captopril (STUDY group=60 patients)** or the **Conventional therapy (CONTROL group=40 patients)** and were subdivided in to four groups as: younger (60years old and below) STUDY group (**Group A=30**), younger control group (**Group B=20**), elderly (60-70 years old) STUDY group (**Group C=30**) and elderly control group (**Group D=20**). Captopril (6.25mg) was given orally immediately after the admission followed by maintaining dose of 12.5-25 mg t.d.s, prescribed while keeping the blood pressures accordingly. No participant had any severe extra-cardiac disease manifestation which could affect the prognosis. Patients with hypotension (Systolic B.P< 90mmHg), cardiogenic shock and severe hypertension (Systolic B.P> 200 mm Hg and/or Diastolic pressure >120 mm Hg) were excluded.

Medications and cardiac events including congestive cardiac failure, fatal arrhythmias, reinfarction and sudden cardiac deaths were continuously monitored among all these groups. Severe arrhythmias like ventricular tachycardia, flutter or fibrillation, sinus arrest, sinoatrial block and complete atrio-ventricular blocks were specifically focused in the trial. Significant pathological coronary arterial stenosis (above 70% luminal diameter) was assessed by arteriography. Ejection fraction (EF) was measured by two-dimensional echocardiography. The two main groups and four subgroups were statistically compared by using ANOVA, Chi-square and Student't test. Variables affecting the efficacy of Captopril were defined in terms of age, sex, familial predisposition, smoking, hypertension, diabetes mellitus, hyperlipidemias, renal diseases, peak Creatinine phosphate kinase (CPK-MB)/troponin T levels, LV ejection fraction, timing of infarct, site of infarction, thrombolytic therapy, beta-blocker, and antiplatelet drugs. All the analyses were performed statistically and a probability (P) of <0.05 was considered significant.

## Results

Systolic blood pressure in 60 patients receiving Captopril was significantly lower than in 40 patients (**Table 1 and Table 2**) who got the conventional therapy only (135.6 ±14.4mmHg/82.8 ±10.3mmHg vs. 144.1 ±18.8mmHg/83.2 ±11.3mmHg, P<0.05). Medications with baseline clinical characters were similar in all the four groups.



Table-1. Blood Pressure (B.P) of Captopril (STUDY) and Conventional Therapy (CONTROL) group

PARAMETERS	CAPTOPRIL (STUDY) GROUP	CONVENTIONAL THERAY(CONTROL) GROUP
No. of Participants	60	40
Sys.B.P (mmHg)	135.6±14.4	144.1±18.8
Mean B.P (mmHg)	134.22	146.46
Standard deviation (S.D)	7.94	10.08
Variance S.D	63.09	101.78
Population S.D	7.87	9.96
Variance Population S.D	62.04	99.23

Table-2. ANOVA Analysis of Systolic B.P of Study and Control group

ANOVA (Sys.B.P)	Sum of squares	df	Mean square	Fisher F-value	P-significance
Between the groups	3,595.622	1	3,595.622	45.868	Significant P<0.05
Within the groups	7682.222	98	78.390		
Total	11,277.844	99			

Regarding medications and other characters (**Table 3**), 18 patients (60%) in Group A, 8 (40%) in Group B, 16 (53.4%) in Group C, and 10 (50%) in Group D took oral aspirin (P>0.05). Moreover, 17 patients (56.7%) in Group A, 7 (35%) in Group B, 14 (46.7%) in Group C, and 6 (30%) in Group D took oral beta-blockers (P>0.05). 16 patients (53.4%) in Group A, 9(45%) in Group B, 14 (46.7%) in Group C, and 7 (35%) in Group D (P >0.05) received thrombolytic therapy. The LV ejection fraction in Group A, B, C, and D were 53.9% ±12.8%, 53.2% ±12.9%, 54.8% ±14.2%, and 55.1% ±14.7% respectively ( P>0.05). Rate of patency of the related artery with thrombolytic therapy was 47.1%, 47.5%, 48.1%, and 40.9% among group A,B,C and D respectively (P>0.05). Hospitalization time in Groups A and B was almost similar (28 ±12 days v s. 30 ±9 days, P>0.05) with similarity in the time of hospitalization among Groups C and D (29 ±10 days vs. 28 ±11 days, P>0.05).Overall 4 patients in the study group and 9 patients in control group died within the hospital (6.67% vs. 22.5%, P<0.0001).Careful data analysis suggested that the survival of patients on Captopril correlated significantly with age (P<0.001). 1 patient in Group A and 1 patient in Group B (3.33% vs. 5%, P>0.05), 3 patients in Group C and 8 patients in Group D (10% vs. 40%, P<0.0001) died. Other multivariates statistically significant

were smoking (P<0.01), beta-blocker (P<0.005), peak CPK (P 0.005), and the intravenous thrombolysis (P 0.01).

Table-3. Result Summary of Subgroups

N	Result Characteristics	Group A	Group B	Group C	Group D
1	Total No. of Patients(n)	30	20	30	20
2	Received Oral Aspirin (n)	18	8	16	10
3	Received B-blockers(n)	17	7	14	6
4	Received Thrombolysis(n)	16	9	14	7
5	LV Ejection fraction	53.9%±12.8 %	53.2%±12.9 %	54.8%±14.2 %	55.1%±14.7 %
6	Hospital stay(Days)	28 ±12	30 ±9	29 ±10	28 ±11
7	Hospital Deaths(n)*	1	1	3	8
8	Artery Patency rate (With Thrombolysis)	47.1%	47.5%	48.1%	40.9%

\*Hospital deaths were statistically significant with \*P <0.05

Group A: Younger Study group  
 Group B: Younger Control group  
 Group C: Elderly Study group  
 Group D: Elderly Control group

### Discussion

Our study clearly reflected that the early effects of Captopril treatment among patients with acute myocardial infarction definitely varied with respect to age. Captopril has a minor effect on younger patients (60 years old and less) and an extremely beneficial effect on elderly patients (60-70 years old) during the hospitalization. On one side, the overall survival rate was lower among elderly patients than that of younger ones in hospitalization phase regardless of the fact, whether Captopril was taken or not. But the most significant finding is that the increased survival after taking Captopril was higher in elderly patients than in younger patients. Captopril protects the ischemic and infarcted zone of injured myocardium after the myocardial infarction and markedly enhances the survival of old aged patients. Treatment with Captopril is definitely associated with improved short as well as long term cardiac prognosis and markedly. Captopril therapy is associated with improved long term prognosis and reduced cardiac mortality during



the hospitalization phase of the therapy and recovery period.

Beta-blockers like metoprolol also enhance its efficacy and beneficial effects. Captopril decreases the fatal life threatening repetitive ventricular arrhythmias and catecholamine levels during acute thrombolytic phase of myocardial infarction providing the evidence that a proper dose of beta-blocker might further help patients taking Captopril in the early hospitalization phase of the recovery among patients with acute myocardial infarction<sup>8</sup>.

Also Captopril exerts beneficial effect in reducing the number of complex ventricular arrhythmias in post-myocardial ischemic patients accompanied by left ventricular dysfunction, mediated via alterations in left ventricle remodeling<sup>19</sup>. The study positively concludes that ACE inhibitors like Captopril in proper dosage play a real vital beneficial role among elderly patients as compared to the younger ones during hospitalization phase of recovery after acute myocardial infarction.

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**CONFLICTS OF INTEREST**

None