Original Article

A Comparison of Early Echocardiographic Findings in Patients having First Acute Myocardial Infarction with or without Pre-Infarct Angina

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Background: Acute myocardial infarction (AMI) is the most common cause of morbidity and mortality. In order to reduce myocardial infarct size, a new technique i.e. ischemic pre-conditioning has evolved. The brief periods of ischemia followed by reperfusion appear to pre-condition the heart and make it more resistant to a subsequent longer period of ischemia. Pre-conditioning is defined as "a rapid, adaptive response to a brief ischemic insult, which slows the rate of cell death during a subsequent, prolonged period of ischemia."

Material & Methods: A comparative study was conducted to identify the patients of AMI with or without pre-infarction angina, to find out the differences in their in-hospital course and to assess the prognostic value of pre-infarction angina in first episode of AMI during hospital stay.

Results: Twenty-five patients with (Group A) and 25 patients without (Group B) pre-infarction angina were compared for their in-hospital course. Mean age ± SD in Group A was 55 ± 7 years and in Group B 54 ± 8 years. There were 18 (72%) males and 7 (28%) females in Group A, and 17 (68%) males and 8 (32%) females in Group B. As far as the baseline risk factors in two groups were concerned, 5 vs 7 patients had diabetes mellitus, 7 vs 8 had hypertension, 16 (64%) vs 13 (52%) were smoker, 3 vs 4 had obesity, 4 vs 5 had family history of IHD and 5 vs 6 had hyperlipidemia in Group A and Group B respectively. Regarding the intake of anti-anginal medication like calcium channel blockers, beta-blockers and nitrates in the two groups, there were more patients in Group A as compared to B who were taking them ($p<0.05$). Similarly there were also 10 (40%) vs 2 patients in Group A and B respectively who were taking aspirin ($p<0.05$). In-hospital complications like cardiogenic shock, CCF, LVF, RVF, recurrent ischemic pain, infarct extension and rhythm abnormalities were more in Group B as compared to Group A ($p<0.05$). When echocardiography was performed, the data showed that the ejection fraction percentage (mean ± SD) in Group A was 55% ± 7.8 versus 44% ± 7.9 in Group B ($p<0.001$). There were 3 in Group A vs 13 patients in Group B who had developed aneurysm ($p<0.05$), 2 in Group A vs 1 in Group B who had papillary muscle rupture, 1 in Group A vs 5 in Group B who developed VSD and 4 in Group A vs 10 in Group B who had clot in left ventricle. While in-hospital mortality between two groups was observed, there was only 1 in-hospital death in Group A vs 6 (24%) in Group B ($p<0.05$).

Conclusion: The presence of pre-infarction angina had a favorable effect on in-hospital course after AMI i.e. a lower incidence of in-hospital mortality, a lower incidence of in-hospital complications, development of significantly smaller infarct size with a higher ejection fraction and a lower incidence of aneurysmal formation.

Keywords: AMI, Angina, Infarction, Pre conditioning

Introduction

In the history of attempts to reduce myocardial infarct size only few therapies have stood the test of time, one is reperfusion and the other is pharmacologic therapies such as calcium channel blocking agents, beta adrenergic blocking agents, oxygen radical scavenging agents and neutrophil inhibitors, and the newest technique for reducing the size of myocardial infarction is ischemic pre-conditioning.[1]

The brief periods of ischemia followed by reperfusion appeared to pre-condition the heart and making it more resistant to a subsequent longer period of ischemia.[2] Pre-conditioning is defined as "a rapid, adaptive response to a brief ischemic insult, which slowed the rate of cell death during a subsequent, prolonged period of ischemia." It has been seen that pre-infarction angina has the potential

to pre-condition the heart; one would predict that it would do so only in infarcts that had been reperfused.[3] Pre-conditioning protects myocardium against a greater subsequent ischemic insult with less threat of infarction.[4] It has been seen that patients with pre-infarction angina may suffer from a less severe infarct than those thought to undergo sudden coronary occlusion without the opportunity for pre-conditioning.[5]

It has also been seen that patients with AMI have a lower in-hospital death rate if they have a history of angina within the 48 hours period that precedes infarction.[6] Patients having the history of pre-infarction angina presenting with first AMI has been reported to be associated with lower in-hospital incidence of sustained ventricular arrhythmias, a lower incidence of pump failure, a lower incidence of cardiac mortality, higher ejection fraction, smaller end-diastolic volume and a lower incidence of aneurysm formation.[7] There is also lower incidence of cardiogenic shock and reduction in in-hospital death from acute anterior myocardial infarction in patients having pre-infarct angina, which is contributing factor in development of collateral circulation.[8] It has been seen that previous angina before non-thrombolized AMI is a marker of increased risk of infarct extension, recurrent ischemic pain and mitral regurgitation.[9]

Aims & Objectives

To find out the differences in Echocardiographic abnormalities in patients having first AMI with and without pre-infarction angina or ischemic pre-conditioning.

Material & Methods

Inclusion Criteria

Both men and women of any age presenting with first episode of AMI with or without pre-infarction angina were included.

Exclusion Criteria

Patients with evidence of old myocardial infarction.

Patients presenting with chest pain, which later on proved to be non-cardiac in origin.

Patients unable to provide a clear clinical history regarding presence or absence of pre-infarction angina.

Method

The study was conducted in East Medical Ward of Mayo Hospital, Lahore. Patients were admitted through emergency. This was a comparative prospective study of 50 patients having their first presentation with AMI with and without pre-infarction angina. Twenty-five patients with and 25 patients without pre-infarction angina were compared for their in-hospital course. The diagnosis of AMI was established on any two of the three criteria i.e., history of chest pain suggestive of cardiac origin, an ECG criteria of an abnormal ST-segment elevation of 1mm above isoelectric TP segment measured at J point in two or more than two contiguous leads in the absence of left bundle branch block (LBBB) or ventricular rhythm, and elevated cardiac enzymes. After establishing the diagnosis all such patients were admitted in CCU and ICU attached with East Medical Ward. A very careful history was taken for the presence and absence of pre-infarction angina, which was defined as presence of typical chest pain occurring at rest or during exercise and relieved by rest or sublingual nitroglycerin.[7] The patients were grouped into two, group A patients having pre-infarction angina and group B patients without it. These patients were monitored continuously throughout their admission on ECG monitor and their in-hospital course was clinically evaluated on twice daily basis along with full ECG recording. The variables assessed in each and every admitted patient were age, gender, presence of coronary risk factors (diabetes mellitus, hypertension, smoking, obesity, family history of IHD, hyperlipidemia, asthma), previous use of anti-anginal medicines, time from onset of pain to presentation to hospital, use of thrombolytic therapy, incidence of in-hospital complications like cardiogenic shock, congestive cardiac failure (CCF), left ventricular failure (LVF), right ventricular failure (RVF), rhythm abnormalities, recurrent ischemia and infarct extension, on echocardiography (left ventricular ejection fraction, aneurysm formation, papillary muscle rupture, ventricular septal defect (VSD) and clot in left ventricle (LV) and in-hospital mortality.

Regarding above variables following investigations were specifically done:

- A bedside monitor was connected with the patients to monitor ECG continuously for detection of any arrhythmia.
- 12 lead ECG.
- Initial cardiac enzymes.
- X-ray chest P. A. view.
- Echocardiography.

Results

Mean age±SD in Group A, comprising of 25 patients

having history of pre-infarction angina, was 55 ± 7 years and in Group B comprising of 25 patients without history of pre-infarction angina, was 54 ± 8 years (p>0.5). There were 18 (72%) males and 7 (28%) females in Group A, and 17 (68%) males and 8 (32%) females in Group B. The p value among males in two groups is >0.5 and among females is >0.5.

As far as the baseline risk factors in two groups were concerned, 5 (20%) vs 7 (28%) patients had diabetes mellitus (p>0.5), 7 (28%) vs 8 (32%) had hypertension (p>0.5), 16 (64%) vs 13 (52%) were smokers (p>0.5), 3 (12%) vs 4 (16%) had obesity (p>0.5), 4 (16%) vs 5 (20%) had family history of ischemic heart disease (p>0.5) and 5 (20%) vs 6 (24%) patients had hyperlipidemia (p>0.5) in Group A and Group B respectively.

No patient in Groups A and B had history of asthma in this study **(Fig-1)**. Regarding the intake of anti-anginal medication in the two groups, there were 14 (56%) vs 4 patients were taking calcium channel blockers in Group A and Group B respectively (p<0.05).

There were 13 (52%) vs 3 patients who were taking beta-blockers in Groups A and B respectively (p<0.05). There were 10 (40%) vs 2 patients in Groups A and B respectively who were taking nitrates (p<0.05). Similarly there were also 10 (40%) vs 2 patients in Groups A and B respectively who were taking aspirin (p<0.05) **(Table 1)**.

When time from onset of pain to presentation was observed, the mean ± SD of hours in Group A was 3.6 ± 2.1 vs 1.6 ± 0.6 hours in Group B (p<0.001). The range in Group A was 0.55 to 8.00 hours vs 0.87 to 7.50 hours in Group B **(Table 2)**.

In-hospital complications in the two groups were as follows: 1 in Group A vs 6 patients in Group B (p<0.05) had cardiogenic shock, 1 in Group A vs 6 in Group B (p<0.05) had CCF, 2 in Group A vs 8 in Group B (p<0.05) had LVF, and 1 in Group A vs 2 patients in Group B (p>0.5) had RVF **(Table 3)**.

2 patients in Group A vs 8 (32%) patients in Group B (p<0.05) had recurrent ischemic pain, 1 in Group A vs 6 (24%) in Group B (p<0.05) had infarct extension and 2 in Group A vs 8 (32%) in Group B (p<0.05) had rhythm abnormalities **(Table3)**.

When echocardiography was performed the data showed that the ejection fraction percentage mean ± SD in Group A was 55% ± 7.8 versus 44% ±7.9 in Group B (p<0.001), **(Table 4)**.

There were 3 (12%) in Group A vs 13 (52%) patients in Group B who had developed aneurysm (p<0.05), 2 in Group A vs 1 in Group B who had papillary muscle rupture (p>0.5), 1 in Group A vs 5 in Group B who developed VSD (p>0.1) and 4 in Group A vs 10 (40%) patients in Group B who had clot in left ventricle (p>0.1) **(Table-4).**

While in-hospital mortality between two groups was observed, there was only 1(4%) in-hospital death in Group A vs 6 (24%) in Group B (p<0.05) **(Fig- 2)**.

Table-1: Differences in intake of anti-anginal medication.

Anti-anginal drugs	Group-A No. %	Group-B No.%	p-value
Calcium Blockers	14 (56%)	4 (16%)	<0.05
Beta Blockers	13 (52%)	3 (12%)	<0.05
Nitrates	10 (40%)	2 (08%)	<0.05
Aspirin	10 (40%)	2 (08%)	<0.05

Table-2: Differences in time from onset of pain to presentation.

	Group-A	Group-B	p-value
Mean± SD (hours)	3.6±2.1	1.6±0.6	<0.001
Range (hours)	0.55-8.0	0.87-7.50	

Table-3: In-hospital complications.

Complications	Group-A No. %	Group-B No.%	p-value
Cardiogenic Shock	01 (4)	06 (24%)	<0.05
CHF/CCF	01 (4)	06 (24%)	<0.05
LVF	02 (8)	08 (32%)	<0.05
RVF	01 (4)	02 (08%)	>0.05
Recurrent Pain	02 (8)	08 (32%)	<0.05
Infarct extension	01 (4)	06 (24%)	<0.05
Arrythmias	02 (8)	08 (32%)	<0.05

Table-4: Echocardiographic data.

Echocardiography	Group-A	Group-B	p-value
EF % (Mean±SD)	55±7.8	44±7.9	<0.001
Aneurysm (n & %)	03 (12%)	13 (52%)	<0.05
Papillary rupture (n&%)	02 (08%)	01 (04%)	>0.5
VSD (n & %)	01 (04%)	05 (20%)	>0.1
Clot in LV (n & %)	04 (16%)	10 (40%)	<0.1

Fig-1: Baseline risk factors differences.

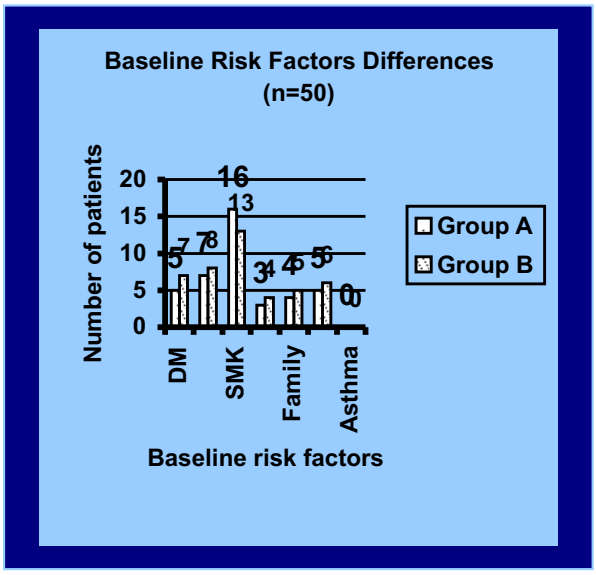
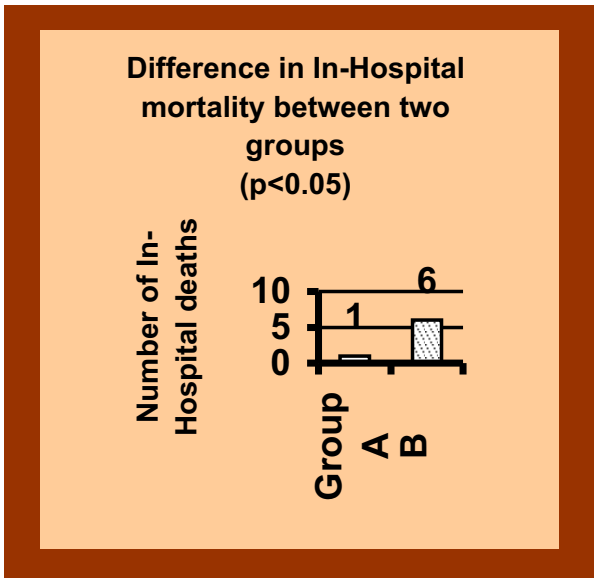


Fig-2: Difference in In-hospital mortality between two groups (p<0.005).



Discussion

Pre-infarction angina before an episode of AMI has a favorable prognostic impact on in-hospital course due to the effect of ischemic pre-conditioning, which is now powerful and reproducible method of delaying cell necrosis. The clinical observation of pre-conditioning would have important therapeutic implications because once its mechanism is elucidated, it may form the basis for new therapies in cardiovascular medicine.[1]

In this study, out of total 50 patients, 25 patients with history of pre-infarction angina were compared with 25 patients without pre-infarction angina before the first episode of AMI. There were no significant differences between the two groups in respect of age, gender and baseline risk factors. This finding is comparable with previous studies.[6-7] There was a statistically significant difference ($p<0.05$) between the two groups regarding the intake of anti-anginal medication before first AMI. The patients with pre-infarction angina were on anti-anginal medication (calcium channel blockers, beta blockers, nitrates and aspirin), which was comparable with the study done by Kloner et al.[6]

The time from onset of chest pain to hospital presentation in patients with angina was longer as compared to patients without angina. This delay may indicate that possibly patients experiencing chest pain become accustomed to it, so it may take him or her longer to come to the hospital after the onset of the chest pain of myocardial infarction. This was also more or less equal to same study mentioned above.[6]

When in-hospital complications were compared, there was statistically significant difference between patients of two groups as far as cardiogenic shock 1 (4%) vs 6 (24%) patients, CCF, 1 (4%) vs 6 (24%) and LVF, 2 (8%) vs 8 (32%) patients were concerned. The patients with a previous history of angina were less likely to develop cardiogenic shock, CCF and LVF as compared to patients without previous history of angina. This was more or less equal to the previous studies.[8,10] There was no statistically significant difference amongst those patients who developed RVF having pre-infarct angina versus those without it. It was probably because of small number of patients who developed RVF in this study.

There was statistically significant difference in patients with previous history of angina versus without angina who developed recurrent ischemic pain i.e. 2 (8%) vs 8 (32%), infarct extension[6] 1 (4%) vs (24%) and rhythm abnormalities 2 (8%) vs 8 (32%) patients. The patients without pre-infarction angina were more likely to develop recurrent ischemic pain ($p<0.05$) and infarct extension ($p<0.05$) as also shown by previous studies because of the fact that patients with pre-infarction angina have more multivessel coronary artery disease.[6-7,9,11-12] The rhythm abnormalities were seen in less number of patients who had previous history of angina before infarction as compared to patients who had no pre-infarct angina ($p<0.05$). Thirty two percent patients in Group B having no previous history of angina developed more malignant arrhythmias like ventricular fibrillation and sustained ventricular

tachycardias comparable more or less with previous studies.[7-8]

The limitation of infarct size was seen in those patients who had history of pre-infarct angina as compared to those who had no pre-infarct angina. There was statistically significant difference in ejection fraction of patients with pre-infarct angina versus without it. The patients with history of pre-infarct angina had greater percentage of ejection fraction as compared to patients with no history of angina before infarction ($p<0.001$). This showed that patients with pre-infarct angina versus without it had got lesser infarct size, low incidence of pump failure, low incidence of aneurysmal formation and low incidence of cardiac rupture, comparable more or less with previous studies.[5,7] There was statistically significant difference ($p<0.05$) in patients with previous history of angina versus no angina who developed aneurysm formation. The patients with preceding angina had low incidence of aneurysm formation as compared to those patients who had no preceding angina.

There was statistically insignificant difference between patients with pre-infarct angina versus without it who developed Papillary Muscle Rupture (PMR) in contradiction to previous study because here all patients were given thrombolysis.[9]

There was also statistically insignificant difference between patients with pre-infarct angina versus without it who developed VSD, corresponding with the result shown by Kloner et al, and did not correspond with the study of Anzai et al because in this study the sample size was small.[7, 9] There was statistically insignificant difference in the development of left ventricle clot after AMI between patients with pre-infarction angina or without it.

There was statistically significant difference ($p<0.05$) between patients having pre-infarction angina versus no pre-infarct angina regarding in-hospital mortality. There was low incidence of in-hospital mortality seen in patients having pre-infarction angina 1 (4%) as compared to patients with no pre-infarction angina 6 (24%). This was comparable more or less with previous studies.[6-7]

All these findings suggest that pre-infarct angina has a protective effect against myocardial damage after abrupt coronary occlusion. The presence of pre-infarction angina was associated with a lower incidence of in-hospital complications and mortality. Multivariate analyses revealed that the absence of pre-infarction angina was an independent predictor of in-hospital cardiac mortality. The potential mechanisms of cardioprotection by previous angina are still debatable. However, some authors observed that patients who experienced angina for more than 1 week before coronary occlusion had greater number of collateral development. This finding was also confirmed by other studies as well.[8,13] The presence of collateral vessels could not be examined in this study due to poor compliance of patients and non-availability of 24 hours angiography facility in this set up.

The other potential mechanism of better effects of previous angina on in-hospital outcome was the use of anti-anginal medication.[6] This finding had been observed in this study as well. Another mechanism of better in-hospital outcome in patients with preceding angina before AMI is ischemic pre-conditioning. This phenomenon is observed by many experimental models.[1-4] This had also been seen by different variables in this study as well. Yet another interesting mechanism was the difference in intrinsic thrombolytic systems in patients with pre-infarction angina. Re-perfusion was achieved more rapidly in patients with pre-infarction angina history.[14] This observation was not studied because of the economic factors and non-availability of more advanced bio-chemical laboratory facility in this set up.

Conclusion

The presence of pre-infarction angina had a favorable effect on in-hospital course after AMI i.e. a lower incidence of in-hospital mortality, a lower incidence of in-hospital complications, development of significantly smaller infarct size with a higher ejection fraction and a lower incidence of aneurysmal formation.

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