



## COMPARE THE INTRACORONARY INFUSION AND DISTAL MICROCATHETER INFUSION OF SODIUM NITROPRUSSIDE DURING PERCUTANEOUS CORONARY INTERVENTION TO PREVENT THE SLOW BLOOD FLOW OR NO-REFLOW IN ACUTE MYOCARDIAL INFARCTION

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### ABSTRACT

**Objective:** The aims of treatment of ST-Segment elevation myocardial infarctions are vessel recanalization and restore the normal coronary blood flow. The no-reflow or slow blood phenomenon is one of the common and critical occurrences after PCI in STEMI patients, unstable angina and coronary total occlusion in which myocardial reperfusion therapy does not restores the optimal level of blood flow. There are several predisposing factors of slow blood flow after PCI have been identified. Sodium Nitroprusside have beneficial effects on fibrinolysis, vasodilatation and disaggregation. Distal micocather infusion have better outcome than intracoronary infusion of sodium nitroprusside before the stent implantation during PCI in patient With STEMI.

**Method:** A prospective observational study was carried out at cardiology department of the First People's Hospital of Jingzhou, which is a first clinical hospital of Yangtze University on patients undergoing intracoronary infusion and distal micocather infusion of sodium nitroprusside during PCI of patient of STEMI with permanent. Variables were recorded at 0 (baseline) and at 3 month follow-up. At 3-month follow-up data of 30 patients on intracoronary infusion group and 30 patients on distal micocather infusion used for final analysis. Variables like, TIMI Blood flow, LVEF, Full restoration of ST-segment, mortality, hospital stay, were compared and analyzed.

**RESULTS:** The mean ages of group MCI and group CON were 65±7.6 and 67.2±5.3 years, respectively, and most of patients were men (70% in MCI and 66.7 % in CON group). Post procedural good flow was achieved in 80.0% patients of distal micocather infusion of sodium nitroprusside and 50 % of the patients have good blood flow when intracoronary infusion groups, respectively (P = 0.307). There was significant difference between the groups in no-reflow assessment.

**Conclusion:** Distal micocather infusion of sodium nitropruside have better outcome than intracoronary infusion of sodium nitropruside before the implantation of stent during primary PCI in patients with acute ST-elevation myocardial infarction (STEMI).

**Keywords:** No-Reflow phenomenon, acute myocardial infarction, percutaneous coronary intervention, Angiography.

**Abbreviation:**

Term	Description
AMI	Acute myocardial infarction
AHA	American heart association
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
ECG	Electrocardiogram
IL-6	Interleukin-6
LVEF	Left ventricular ejection fraction
MCI	Micocather infusion group
PCI	Percutaneous coronary intervention
STEMI	ST-Segment elevation myocardial infarction
SBP	Systolic Blood pressure
UA	Unstable angina

## INTRODUCTION

**Background:**

**Introduction to Cardiovascular disease:**

Cardiovascular diseases (CVD) are one of the main concerns in medical field in the recent decades. With growing technologies, it is still a major cause of morbidity and mortality. In recent due to multiple factors, incidence and prevalence of cardiovascular disease is still at large around the world. In past, cardiovascular illness was considered to be disease of developed countries. But at present it is all around the world and now increasing in developing countries. Cardiovascular diseases are the leading cause of death around the world now a day. With growing development in technology, medication and procedures, death rates have been lowered significantly in developed countries and it is still common at developing countries. Cardiovascular diseases commonly are conduction abnormalities (arrhythmias), coronary artery disease (myocardial infarction), heart failure and valvular heart disease. Among all deaths, cardiovascular disease death believed to be around 35% and among these 1 million deaths is sudden death. Cardiovascular disease has become the most important and largest cause of non-communicable disease deaths worldwide at over

50%.

Cardiovascular illness is consisted of vessel related (coronary arteries disease), conduction abnormalities (cardiac arrhythmias), structural (valvular heart disease), functional (heart failure) etc. Diagnosis of the disease has become easy and quality of life has been improved and death is delayed with improved intervention with medication, treatment and interventional procedures. Electrocardiogram and echocardiography has played important role in diagnosis of cardiovascular illness. Though there are still much to do in cardiovascular disease but medical science has shown great advancement in treating cardiovascular illness. Interventional cardiology, percutaneous coronary intervention (PCI), implantable cardiovascular devices (pacemakers and defibrillators) is recent updates in late 20th and early 21st century. Coronary artery disease (CVD) and Cardiac arrhythmia are common disease in cardiovascular system. All the diseases are interconnected in cardiovascular system that one kind of illness can give rise to other illness within the same system. When there is a problem in coronary artery (stenosis or blockage due to thrombus) coronary artery disease that is myocardial infarction will occurs similarly when there is problem in heart conduction system, cardiac arrhythmia occurs in which heart beats too slowly, too fast or irregularly. Consequences of arrhythmias can be both fatal at initial stage and progressively deteriorating. Bradycardia and tachycardia are common terms used with abnormal heart rhythm. The National Institutes of Health defines bradycardia as a heart rate <60 bpm in adults other than well trained athletes. However, population studies frequently use a lower cutoff of 50 bpm for bradycardia [3]. When heart rate is higher than 100 beats per minute then it is termed as tachycardia. Heart requires regular and uninterrupted signal to work properly and when any illness or condition disrupts this signal further deterioration of cardiac functions starts.

### **Basic anatomy of the heart:**

Heart plays a very important role in human body. The main function of heart is to pump blood which carries essential nutrient and oxygen. Heart is a hollow muscular organ slightly larger than a closed fist situated within the pericardium in the middle mediastinum. The weight of the heart is about 250-300 grams. Stern costal and diaphragmatic surfaces are the two surfaces of the heart whereas it has three borders; right border, left border and inferior border. Heart consists of four grooves.

Pericardium is external layer and it has double walled sack, which is composed of a superficial fibrous pericardium and deep two layered serous pericardia. The deeper serous pericardium contains two layers, parietal and visceral layer. The main function of the pericardium is to protect and anchorage of the heart, prevent over flowing of the heart with the blood and allowing heart to conduct its function in relatively non-friction condition. Myocardium is middle layer consisting muscle and it makes most part of the heart. Innermost layer of the heart is endocardium which is a layer of endothelial.

### **Atria of the heart:**

Atria are the chambers that receive blood from the systemic circulation through superior and inferior venacava and atrium also receives oxygenated blood from lung. Two atria are separated by interatrial septum and each atrium has a protruding auricle. Blood collected in the atria are then pumped

into ventricles.

### **Ventricle of the Heart:**

There are two ventricles in the heart, right ventricle and left ventricle. These are the chambers that distribute the blood from the heart. These two walls are separated by an interventricular septum which contains components of conduction system. Deoxygenated blood is pumped to right ventricle by right atria and right ventricle pumps that blood to lung via pulmonary trunk. On the other hand, oxygenated blood collected in left atrium is pumped into left ventricle and then left ventricle pumps it into aorta which circulates to the whole body. Left ventricle has thick myocardium because of greater work load done by left ventricle. Right ventricle supplies to blood to low pressure system which needs less energy output that to be generated by the ventricle whereas left ventricle supplies blood to systemic flow which is a higher pressure system and because this left ventricle needs more forceful contractions. The wall of left ventricle is three times thicker than that of right ventricle.

### **Septum/fibrous skeletal and heart valves:**

Interatrial septum divides two atria. It is situated between right and left atria and contains fossa ovalis. Interventricular septum is situated between right and left ventricle and consists of upper membranous part and thick lower muscular part. Fibrous skeleton is fibrous ring which surround the atria ventricular, pulmonary and aortic orifice. Heart valves help in blood flow in one direction only. Valves consist of endocardium along connective tissue core.

There are two major kind valves; Atrioventricular and Semilunar valves. The valve that makes pathway between two right atria and ventricle is right Atrioventricular valve and the other one is left Atrioventricular valve connecting the other half. Right Atrioventricular valve is tricuspid valve whereas left Atrioventricular valve is bicuspid valve.

### **Blood supply in the heart:**

Heart is supplied with coronary circulation. The right and left coronary artery arises from ascending aorta that supplies blood to the heart. The right coronary artery (RCA) runs through the right Atrioventricular groove and it supplies to right atrium, right ventricle and anteroposterior side of left ventricle. Right coronary artery (RCA) supplies to sinoatrial node about 60% of individuals and the AV node in about 90%. Blockage to supply to these nodes results to conduction delay causing sinus bradycardia and may also cause atrioventricular block. RCA plays important role in heart's conduction system. Left coronary artery then divides to left descending artery (LAD) and left circumflex artery (LCX) at the distance of 2.5 cm from its origin at the root of the aorta. Left descending artery runs through anterior interventricular groove whereas left circumflex runs posterior atrioventricular groove. Anterior part of the septum and the anterior, lateral and apical walls are supplies by LAD whereas circumflex makes marginal branches which supply the lateral, posterior and inferior segments of the left ventricle. The deoxygenated blood is then drained to coronary sinus in Atrioventricular groove when further drains into right atrium.

### **Basic Physiology of the heart:**

Right atrium is filled with deoxygenated blood through superior venae cava, inferior venacava and coronary sinus to the right atria and at the sometimes similar filling is being repeated in left atrium where oxygenated blood pours through pulmonary veins from the lungs. Then the blood passes to respective ventricles and then they are pumped to pulmonary and systemic circulation by right ventricle and left ventricle respectively. Cardiovascular system adapts itself for maintain hemostasis of the body.

### **Cardiac cellular physiology:**

Heart is composed of cardiac muscles which are only found within the heart. Heart muscles are called cardiac myocytes in cellular unit. Action potential in the cardiac muscles generates an impulse that causes contraction and relaxation of heart muscles. Heart also contains a cardiac pacemaker cell that controls the heartbeat. These are special cardiac muscle cells which controls heart contraction. These pacemaker cells also respond signals from autonomous nervous system for increasing or slowing the rate of the heart. These pacemaker's cells constitute a distinct pathway within the heart; the conduction system.

### **Cardiac cycle:**

A complete heartbeat starting from its generation and ending at the starting of next beat, which consists of phases like diastole and systole along with the intervening pause, is a cardiac cycle. The heart rate describes the frequency of cardiac cycle which is commonly expressed as beats/minute. One cardiac cycle consists of two main phases; diastole and the systole. In simple words diastolic is a phase where cardiac muscles relax and refilling of the chamber occurs and systolic is the phase where heart muscles contract and pumps blood to the lung and systemic circulation. This whole process of filling of atria then passing blood to ventricles and then forcefully pumping out of the heart happens in a single cycle which is completed in approximately 0.8 seconds (considering 72 beats in a minute) in healthy heart in normal condition. Flow of blood to the chambers and to the blood vessels all largely depends on the pressure gradient around the chamber and vessels which quickly maintains and repeats in a cardiac cycle. An average human heart beats around 70-72 beats in a minute. With this rate, it takes around 0.8 second to complete a cardiac cycle. In this 0.8 second, 0.1s is of atrial systole, then around 0.3s ventricular systole and last 0.4 s for atrial and ventricular diastole.

### **Phases of cardiac cycle are listed as under:**

#### **Phase 1 (Atrial Contraction):**

Atria contracts and the pressure in the atria increases which makes blood to open atrioventricular valves and fill ventricles with the blood. After completion of atrial contraction, pressure in the atria starts falling which causes reversal of pressure gradient across the atrioventricular valves. This causes valves float upward before closure. This time, volume in the ventricles reach at the maximum level and this is termed an 'end-diastolic volume (EDV). The amount of blood in left ventricular EDV (LVEDV) is around 120 ml.

### **Phase 2 (Isovolumetric Contraction):**

When pressures inside the ventricles are higher than the atria then atrioventricular valves closes. This closure of atrioventricular valve makes first hear sound 'S1'. There is split of around 0.04 sec due to mitral valve closing before tricuspid valve. In time between the closing of atrioventricular valves and opening of aortic and pulmonary valves, the pressure of ventricles increases rapidly despite no change in the ventricular volume (i.e., no filling or ejection). There is no change in the ventricular volume due to closure of all the valves in this phase, that's why it is referred as 'isovolumic' or 'Isovolumetric' contraction.

### **Phase 3 (Rapid Ejection):**

In this phase blood from both the ventricles ejects rapidly towards aorta and the pulmonary arteries. When there is less pressure in aorta and the pulmonary than in the ventricles, aortic and the pulmonary opens and rapid ejection of blood occurs.

### **Phase 4 (Reduced Ejection):**

Ventricular pressure decreases slightly lower than the pulmonary artery and aorta but some outward flow still continues because of blood's kinetic energy. There is gradual increase in left and right atrial pressure due to return of venous blood from the lung and systemic circulation.

### **Phase 5 (Isovolumetric Relaxation):**

At the time when intraventricular pressures lower sufficiently at the end of phase 4, aortic and pulmonary valves close abruptly which makes second heart sound (S2). This begins Isovolumetric relaxation. The volume that is left in the ventricle is known as end systolic volume, which is around 50 ml in left ventricle and the difference between end diastolic volume and endsystolic volume is around 70 ml and that is termed as stroke volume.

### **Phase 6 (Rapid Filling):**

In this phase ventricles continue relaxing from the end of previous phase. This will cause pressure falling below their atrial pressures. This will cause opening of atrioventricular valves and passive ventricular fillings starts. Filling of ventricle is normally silent. If there is any third heart sound (S3) then it may indicate some tensing in chordae tendinea and the atrioventricular ring during relaxation and filling of ventricles. S3 hear sound in children is considered normal whereas it is often pathological in adults due to ventricular dilation.

### **Phase 7 (Reduced Filling):**

With continue filling of ventricles with blood and expansion they become less compliant and there is increase in intraventricular pressures. This increase in pressure in ventricles lowers the pressure gradient across the atrioventricular valves. During rest, ventricle is filled around 90% at the end of phase 6.

### **Conduction system of the heart:**

Autonomous nervous system (ANS) controls the heart. It increases/decreases the contraction but it does NOT initiate it. The heart has its own regulating system which we called the conduction system. The

conduction system consists of specialized muscle a cell that generates action potentials within the cardiac tissue. These special cardiac cells in the cardiac conduction system generate and coordinate the transmission of electrical impulses to myocardial cells. This results in sequential atrioventricular contraction that provides for the most effective flow of blood, thereby optimizing cardiac output. Automaticity, excitability and conductivity are the characteristics of the cardiac conducting cells. Automaticity is the ability of start and electrical impulse with in the heart. Excitability is the ability to respond to the electrical impulse. Conductivity if the ability to transmit the electrical impulse forms on cell to another cell. Components of the conduction system of heart are:

### **SA node (Sinoatrial node):**

It is also labelled as pacemaker of the heart. Situated at the junction of the right atrial appendage with superior venae cava and underlies at the uppermost part of the sulcus terminals. It is 10-20x1x3 mm in size. It is specialized branching of myocardial fibers which are embedded in dense matrix of fibrous tissue. SA is supplied by right coronary artery (55%) and left circumflex branch of left coronary artery (45%). P wave in an ECG is representation of the conduction of impulses in SA node. SA node generates impulses at the rate of 70-80/min. Conduction rate of SA node is 0.05 m/s.

### **Intermodal conduction paths:**

These are special pathways that lie in atrial wall. The function of this path is to transmit impulses from sinoatrial (SA) node to Atrioventricular (AV) node quickly. There are 3 intermodal tracts from SA node to AV node, anterior, middle and posterior. Anterior branch also give rise to Bachmann branch that resides in left atrium. Conduction rate of atrial pathway is 1 m/s.

### **Atrioventricular (AV) node:**

It lies subendocardial in medial wall of right atrium, 1cm above the opening of coronary sinus. It is supplied by right coronary artery (90%) and circumflex branch of left coronary artery (10%). 0.12 second delay in conduction through Atrioventricular (AV) node. AV node generates impulses at the rate of 40-60/min. Conduction rate of AV node is 0.02 - 0.05 m/s.

### **Bundle of HIS:**

Also as Atrioventricular (AV) bundle of his. It is 2-3 cm long which passes in the substance of central fibrous body that reach to lower margin of the membranous part of ventricular septum. PR interval in an ECG is a representation of the conduction of electrical impulses through intermodal tracts. Bundle of HIS generate impulses at the rate of 40/min. Conduction rate of His bundle is 1 m/s.

### **Right bundle branch:**

It is the continuation of bundle of HIS. It is a compact bundle with 1 mm thickness. It is continuous with the fibers of purkinje fibers.

### **Left bundle branch:**

It pierces interventricular septum. Two branches: anterior and posterior. It is continuous with

purkinje plexus of the left ventricle.

### **Purkinje Fibers/ventricular myocardial muscles:**

Both the bundle branch ends to make purkinje fibers. These fibers stimulate groups of cells for myocardial contraction. Electrical activity of purkinje fibers are noted as QRS complex in an ECG. Purkinje system generates impulses at the rate of 24/min. Conduction rate of purkinje system is 1 m/s and ventricular muscle is 1 m/s.

### **Acute myocardial infarction:**

Acute myocardial infarction is a life threatening disease with high mortality. The main cause of acute myocardial infarction is the sudden occlusion of main coronary artery or its branch. Early reperfusion therapy is necessary to restores the normal blood flow, reduces the area of necrotic myocardium and reduces the mortality [1-3]. ST-segment elevation myocardial infarction (STEMI) is defined as combination of chest pain greater than 30 minute, ECG changing with ST-Segment elevation of greater than 2 mm in at least 2 precordial chest leads and greater than 1 mm in limb leads and increased levels of Troponin I or CKMB level higher than twice the upper limit of normal ranges. Primary percutaneous coronary intervention (PCI) is the reperfusion therapy used in treatment of ST-Segment elevation myocardial infarction, unstable angina and coronary total occlusion to prevent the progression of myocardial necrosis [3]. However some patients have no reflow or slow blood flow in related blood vessel after emergency primary percutaneous coronary intervention with stent implantation [3-6].

### **ST-Segment Elevation Myocardial Infarction:**

ST-segment elevation myocardial infarction is one of the most common diagnoses in hospital patients. More than half of the acute STEMI related death occurs before the individual reached the hospital. When patients with prolonged ischemic chest pain or chest discomfort at rest are first seen, the working clinical diagnosis is that they are suffers from acute coronary syndromes. The 12 lead electrocardiograms provide diagnosis and also give decision pathways for management and also help in differentiation of ST-Segment elevation myocardial infarction from those presenting without ST-segment elevation myocardial infarction. Serum cardiac biomarkers are obtained to differentiate unstable angina from non-ST-Segment elevation myocardial infarction (NSTEMI) and to assess the management of ST-segment elevation myocardial infarction.

STEMI occurs when coronary blood flow decrease suddenly after a thrombotic occlusion of a coronary artery, previously affected by atherosclerosis. Slowly developing coronary artery stenosis does not precipitate STEMI because of development of collateral circulation. STEMI occurs when a coronary artery thrombus develops rapidly at a site of vascular injury. This vascular injury is produced by Cigarette smoking, hypertension, diabetes mellitus and lipid accumulation. In most of cases STEMI occurs when surface of an atherosclerotic plaques become disrupted (exposing its content to the blood) and condition favor thrombogenesis. A mural thrombus forms at the site of plaque disruption and coronary artery become

occluded. After an initial platelet monolayer forms at the site of disrupted plaque, various agonists (collagen, epinephrine, serotonin and ADP) promote platelet activation. After agonist stimulation of platelet thromboxane A<sub>2</sub> (vasoconstrictors) is released, further platelet activation occurs and resistance to fibrinolysis develops.

In addition to the generation of thromboxane A<sub>2</sub> activation of platelets by agonists promotes a conformational change in the glycoprotein IIb/IIIa receptor. Once converted to its functional state, these receptors will develop a high affinity for soluble adhesive protein, such as fibrinogen. Fibrinogen binds with two different platelets simultaneously, resulting in platelet cross linkage and aggregation.

The coagulation cascade is activated on exposure of tissue factor in damaged endothelial cells at the site of disrupted. Factor VII and X are activated, leading to conversion of prothrombin to thrombin, which then converts fibrinogen to fibrin. The coronary artery eventually becomes occluded by thrombus containing platelet aggregates and fibrin strand.

In rare case STEMI may occur due to coronary artery occlusion caused by coronary emboli, congenital abnormalities, coronary spasm and variety of systemic inflammatory disease. The amount of myocardial damage caused by coronary occlusion depends on (1) duration of coronary occlusion, (2) demand for oxygen of the myocardium whose blood supply has been suddenly limited, (3) territory supplied by affected vessel, (4) vessel become totally occluded or not, (5) quantity of blood supply by collateral vessel to the affected tissue, (6) endogenous factors that can produce early spontaneous lysis of the occlusive thrombus, (7) the adequacy of myocardial perfusion in the infarct zone when flow is restored in the occluded epicardial coronary artery.

### **Clinical presentation of STEMI:**

**Pain:** most common presenting complaint in patients with STEMI. The pain is deep and visceral and described as a heavy, squeezing and crushing and sometime described as a stabbing or burning in characters. The chest pain is located at the Centre portion of chest or epigastria and pain radiates to left arm most commonly and less commonly to neck, lower jaw, back and abdomen. Pain is associated with autonomic disturbance such as nausea, vomiting, sweating, weakness, anxiety and sense of impending doom. The painless STEMI is greater in patients with diabetes mellitus and older age groups. STEMI may present with sudden onset breathlessness and may progress to pulmonary edema. Other less common presentations with or without pain, sudden loss of consciousness, confusion, sensation of profound sweating, appearance of arrhythmia, evidence of peripheral embolism or drop in arterial pressure.

### **Physical finding:**

Most of the patients are anxious and restless. Coolness of extremity commonly occurs. The combinations of substernal chest pain persisting for greater than 30 minutes and diaphoresis strongly suggest STEMI. Many patients have normal pulse rate and blood pressure within first hours of STEMI. About one-fourth of patients with anterior wall myocardial infarction have sympathetic nervous system activation, which lead to tachycardia and hypertension. Unto one-half with inferior wall myocardial infarction show

evidence of parasympathetic activation, which lead to bradycardia and hypotension. The apical impulse is difficult to palpate. In patients with anterior wall myocardial infarction, abnormal systolic pulsation caused by dyskinesia bulging of infarcted myocardium may develop in periapical area within the first days of illness. Other physical sign of ventricular dysfunction include fourth and third heart sounds and decrease intensity of first heart sounds. Paradoxical splitting of the second heart sound may present. A transient's midsystolic or late systolic apical systolic murmur presents due to dysfunction of mitral valves apparatus. The pericardial friction rub may be heard in patients with transmural STEMI. The carotid pulses have decreased in volume, reflecting reduced stroke volume. The temperature elevated up to 38C during first week after STEMI.

### Laboratory finding:

The laboratory test of value in confirming the diagnosis may be divides into four groups: (1) ECG, (2) serum cardiac biomarkers, (3) cardiac imaging, (4) nonspecific indices of tissue necrosis and inflammation.

**Electrocardiogram:** ECG is usually helpful in confirming diagnosis. Sometime it is difficult to interpret if there is bundle branch block or evidences of previous myocardial infarction. In initial stage of myocardial infarction, ECG produces ST-segment elevation, later on there is diminution in size of R-wave. Most of the patients initially presents with ST-segment elevation, ultimately develop Q-wave on ECG in full thickness MI. subsequently the T-wave becomes inverted. A few patients initially presents with ST-segment elevation, will not develop Q-wave on ECG, when there is not complete obstruction or transient obstruction or rich collateral circulation. Some patients presenting with ischemic discomfort but without ST-segment elevation, if a serum cardiac biomarker of necrosis is detected a diagnosis of NSTEMI is made. A minority of patients, who present initially without ST-segment elevation, may develop Q-wave myocardial infarction. The ECG changes are best seen in the leads that face the infarcted area as shown in table 1.

ST-segment elevation	Myocardial territory	Coronary artery involved
V1-V6 or LBBB	Anterior and septal wall	Proximal LAD or left main
V1-V2	Septum	Proximal LAD or septal branch
V2-V4	Anterior wall	LAD
V5-V6	Lateral wall	LCA
II, III, aVF	Inferior wall	RCA or LCX
I, aVL	High lateral wall	Diagonal or proximal LCX

**Table 1:** Location of myocardial infarction

Serum cardiac biomarkers: certain protein released from necrotic heart muscle after STEMI is called serum cardiac biomarkers. The most commonly used serum cardiac biomarkers in detection of myocardial infarction are creatine kinase (CK-MB) and cardiac specific protein, Troponin T and I. The Troponin is also released in unstable angina with minimal myocardial damage. Serial estimation is helpful because it is the change in plasma concentration of theses markers that is of diagnostic value. CK-MB start to rise in blood at 4-6 hour, peak at 12 hour and fall to normal within 48-72 hours. The most sensitive markers of myocardial cell damage are Troponin T and I, which are released within 4-6 hours and remain elevated for up to 2 weeks in

blood. The American colleges of cardiology and European society of cardiology have redefined myocardial infarction as a typical rise in CK-MB or Troponin T and I, above the 99<sup>th</sup> centile for normal with one of the following feature: Ischemic symptom, development of pathological Q-wave on ECG, ischemic ECG change (ST-segment elevation or depression or coronary artery intervention. The MI is also associated with Polymorph nuclear leukocytosis, which appears within few hour of onset of pain and persists for 3-7 days; the white blood cell count reaches up to level of 12000-15000/ $\mu$ L. The erythrocyte sedimentation rate rise and peak during the first week and remain elevated for 1-2 weeks.

### Cardiac Imaging:

**Echocardiography:** Abnormalities of wall motion on the two dimensional echocardiography is always present. The acute STEMI cannot be differentiated from old myocardial scar or from acute severe ischemia by echocardiography. Echocardiography can be performed at bedside and very useful technique for accessing the left and right ventricular function and for detecting important complication such as mural thrombus, mitral regurgitation, ventricular septal defect, cardiac rupture and pericardial effusion. When ECG is not diagnostic of STEMI, early detection of presence or absence of wall motion abnormality by echocardiography can help in management decision, such as whether patient should receive reperfusion therapy (percutaneous coronary intervention PCI or fibrinolysis).

**Radionuclide imaging technique:** Radionuclide imaging techniques are also available for evaluating patients with suspected ST-Elevation myocardial infarction. These techniques are used less commonly can echocardiography because of lack of sensitivity and specificity. Perfusion scanning is sensitive but it cannot differentiate acute infarcts from chronic scar so not specific for diagnosis of acute myocardial infarction. Radionuclide ventriculography frequently demonstrates wall motion disorders and reduction in ventricular ejection fraction in patients with ST-Segment elevation myocardial infarctions.

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Any one of the following criteria meets the diagnosis of prior myocardial infarction

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- (1) Pathological Q-wave with or without symptom in the absence of no ischemic causes
  - (2) Imaging evidences of a region of loss of viable myocardium that is thinned and fails to contracts, in absence of no ischemic causes
  - (3) Pathologic finding of prior MI
- 

**Table 2:** Criteria for prior myocardial infarction

### Management of myocardial infarction:

**Prehospital care:** The prognosis of STEMI is related to occurrence of the general classes of complication: (1) electrical complication that is arrhythmia and (2) mechanical complication that is pump failure. Most out of hospital death from acute ST-segment elevation myocardial infarction is due to sudden development of ventricular fibrillation. The majority of death due to ventricular fibrillation occurs within 24 hour of onset of symptom and half occurs within first hour. The Prehospital care of patients with suspected ST- segment elevation myocardial infarction include: (1) recognition of symptom by patients and prompt seeking of

medical attention, (2) informed medical care team, which is capable of performing of resuscitative maneuvers, (3) transformation of patients to hospital, where doctors and nurse managed arrhythmia and providing advanced cardiac life support, (4) expeditious implementation of reperfusion therapy. The guidelines for initiation of fibrinolysis in Prehospital setting include ability to transmit 12 lead ECGs to confirm the diagnosis, presence of paramedics in ambulance, training of paramedics in the interpretation of ECGs and management STEMI.

### **Management in emergency department:**

The goal of management of patients with suspected STEMI in emergency department includes, control of cardiac discomfort, rapid identification of patients who are candidates for urgent reperfusion therapy, triage of lower risk patients to appropriate location in the hospital and avoidance of inappropriate discharge of patients with ST-segment elevation myocardial infarction. The main goal is to minimize the time from the first medical contact to initiation of reperfusion therapy. Also involve the transfer the patients from non-PCI hospital to another hospital where percutaneous coronary intervention is possible, with a goal of limiting percutaneous coronary intervention within 120 minute of first medical contact.

**Aspirin:** Aspirin is essential in management of patients with suspected STEMI. Rapid inhibition of cyclooxygenase-1 in platelets followed by reduction of thromboxane A<sub>2</sub> level is achieved by buccal absorption of aspirin of 160-325 mg and then followed by daily administration of aspirin 75-162 mg.

**Sublingual nitroglycerin:** sublingual nitroglycerin 0.4 mg of three doses administer at about 5 minute intervals. Nitroglycerin decreases the myocardial oxygen demands (by lowering preload) and increase myocardial oxygen supply by dilating the infarct related coronary artery or collateral vessel. After giving nitroglycerin, if chest discomfort is still present and evidence showing ongoing ischemia such as further ST-Segment or T-wave shift, intravenous nitroglycerin should be considered. Nitrates should be avoided in patients who present with low systolic arterial pressure (< 90 mm of Hg), or clinical suspicion of RV infarction (inferior infarction on ECG, elevated jugular venous pressure, clear lung and hypotension).

**Morphine:** Morphine is very effective analgesic for pain associated ST-segment elevation myocardial infarction. Morphine reduces sympathetic mediated arterial and venous constriction resulting venous pooling may reduce cardiac output and arterial pressure. Morphine also has vagotonic effect and may causes bradycardia or advanced degree of heart block, mainly in patient with inferior wall myocardial infarctions. Theses side effect responds to atropine 0.5 mg intravenously. Morphine is usually administered small dose (2-4 mg intravenous) in every 5 minutes.

**Beta blockers:** Intravenous beta blockers are also useful in control of pain in ST-segment elevation myocardial infarction by diminishing myocardial oxygen demands. Beta blockers also reduced the risk of reinfarction and ventricular fibrillation. Oral beta blockers should be started within 24 hours, who do not have following, which are listed in **table 3**. A commonly used beta blockers is metoprolol 5 mg every 2-5 minute for total three doses, provide a heart rate > 60 beats/minute, systolic blood pressure > 100 mm of Hg and PR-interval < 0.24 seconds. After the fifteen minute of last intravenous dose, an oral regimen is initiated

of 50 minute every 6 hours for 48 hours followed by 100 mg every 12 hourly.

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In following condition we can't use beta blockers in patients with STEMI

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- (1) Sign and symptom of low cardiac output
  - (2) Sign and symptom of heart failure
  - (3) Increase risk of cardiogenic shock
  - (4) Prolong PR-interval in ECG (> 0.24 seconds)
  - (5) Seconds or third degree heart blocks
  - (6) Active bronchial asthma
  - (7) Chronic obstructive pulmonary disease
  - (8) Reactive airway disease
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**Table 3:** Contraindication of beta blockers in ST-segment elevation myocardial infarction

### Management Strategies:

The primary tool for screening a patients and making decision is the initial 12 lead ECG. When ST segment elevation of at least 2 mm in two contiguous precordial chest lead and 1mm in two adjacent limb lead is present, a patients should be considered for reperfusion therapy. The process of selecting patients for fibrinolysis versus primary percutaneous coronary intervention (angioplasty or stenting) is discussed below. In absence of ST-segment elevation, fibrinolysis is not helpful and may harm the patients.

**Limitation of infarct size:** Unto one third of patients with ST-segment elevation myocardial infarction achieve spontaneously reperfusion of the infarcted related coronary artery within 24 hours and improved healing of infarcted tissue. Reperfusion by percutaneous coronary intervention or by fibrinolysis accelerated the opening of infarcted related coronary artery in those patients in whom spontaneously fibrinolysis ultimately occurred and increase the number of patients in whom restoration of flow in infarcted related artery is accomplished. Protection of the ischemic myocardium by maintain the balance between myocardium oxygen supply and demands through pain control, treatment of heart failure and minimization of tachycardia and hypertension extends the window of time for the salvage of myocardium by reperfusion strategies. Glucocorticoids and non-steroidal anti-inflammatory drugs avoided in STEMI because they can impairs the healing of infarct and increase the risk of myocardial rupture and their use may result increase the size of infarcts. They can also increase the coronary vascular resistance and reduce the flow to ischemic myocardium.

### Primary percutaneous coronary intervention:

Percutaneous coronary intervention (PCI) is usually angioplasty and or stenting without preceding fibrinolysis is referred to primary PCI. PCI is very effective in restoring perfusion in STEMI, when done in emergency within few hours of myocardial infarction. PCI is more effective than fibrinolysis in opening occluded coronary artery and associated with better short term and long term clinical outcomes. Compared to fibrinolysis, primary PCI is preferred when the diagnosis is doubtful, cardiogenic shocks is presents,

bleeding risk is presents, symptom have been presents for at least 2-3 hours when clot is mature and less likely lyses by fibrinolytic drugs. Indication of PCI is listed on table 4. PCI is expensive and its applicability is limited by availability and available only in few hospitals.

---

Following are the indication of primary percutaneous coronary interventions in STEMI

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- (1) Refractory arrhythmia
  - (2) Have a contraindication of fibrinolytic therapy
  - (3) Are at higher risk of death or development of congestive heart failure
  - (4) Under went recent percutaneous coronary intervention or CABG
  - (5) If diagnosis is doubt
  - (6) Cardiogenic shock is presents
- 

**Table 4:** Indication of Primary Percutaneous coronary intervention in patients with STEMI

### **Fibrinolysis:**

The principle goal of fibrinolysis is to restoration of coronary artery patency. If there is no contraindication are present, fibrinolytic therapy should be initiated within 30 minute of presentation that is door to needle time is  $\leq 30$  minute and some of indication of fibrinolytic therapy are listed in table 5. The fibrinolytic agents used are tissue plasminogen activators, streptokinase, Tenecteplase and reteplase. These drugs act by promoting the conversion of plaminogen to plasmin, which lyses fibrin thrombi. When assessed angiographically, flow in culprit coronary artery is described by simple qualitative scale called Thrombolysis in myocardial infarction(TIMI)grading system which is described in table 6. The goal of reperfusion therapy, because full perfusion of infracted related coronary artery have better result in term of limiting size of infarct, maintains left ventricular functions and reduction in both short term and long term mortality rates. Tissue plaminogen activators and Tenecteplase are effective that streptokinase for restoring full perfusion that is TIMI grade 3 coronary flow.

---

Following are the indication of fibrinolytic therapy

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- (1) Acute chest discomfort characteristic of myocardial infarction.
  - (2) ECG criteria for ST-segment elevation myocardial infarction.
    - ST elevation  $\geq 1$  mm in at least two lead off either
      - Inferior wall II, III and aVF.
      - Lateral group: I, aVL, V5 and V6.
    - ST elevation  $\geq 2$  mm in at least two contiguous anterior lead (V1-V4).
    - New Left bundle branch block.
  - (3) Primary PCI is not available or delay to PCI from first medical contact would be  $> 120$  minute.
- 

**Table 5:** selection criteria of Fibrinolytic therapy

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Following are the grading of Thrombolysis in myocardial infarction grading system

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- (1) Grade 0: Complete occlusion of infarcted coronary artery
  - (2) Grade 1: Some penetration of contrast material beyond the point of obstruction but without perfusion of distal coronary bed
  - (3) Grade 2: Perfusion of entire infarct vessel into distal bed but flow is delayed compared with that of normal artery
  - (4) Grade 3: Full perfusion of the infarct vessel with normal flow
- 

**Table 6:** Thrombolysis in myocardial infarction (TIMI) grading system

The current recommended regimen is tissue plasminogen activators (tPA) consist of 15 mg bolus followed by 50 mg intravenous over 30 minute followed by 35 mg over next 60 minute. Streptokinase IS administered at 1.5 million unit's intravenous over one hour. Tenecteplase (TNK) is given as a single weight based intravenous bolus of 0.53mg/kg over 10 seconds. In some of the conditions we can't use fibrinolytic agent which are listed in table 7. Allergic reaction to streptokinase occurs in 2 % of patients who used streptokinase and hypotension occurs up to 10 % of cases. Hemorrhage is the most frequently and most serious complications occur during fibrinolysis. Hemorrhagic stroke is most serious complication occur up to 0.9 % of patients.

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Following are the contraindication of fibrinolytic agents

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- (1) Absolute contraindication of thrombolytic therapy:
    - History of cerebrovascular hemorrhage at any time
    - No hemorrhagic stroke or other cerebrovascular event within past years
    - Marked hypertension (SBP=  $\geq 180$  mm of Hg or DBP=  $\geq 110$  mm of Hg)
    - Suspicion of aortic dissection
    - Active internal bleeding
  - (2) Relative contraindication of thrombolytic therapy:
    - Current use of anticoagulants (INR=  $\geq 2$ )
    - Recent (< 2 weeks) invasive or surgical procedure
    - Prolonged Surgical procedure (> 10 minute)
    - Cardiopulmonary resuscitation
    - Pregnancy
    - Hemorrhagic ophthalmic conditions
    - Active peptic ulcers disease
    - History of several hypertensions
- 

SBP= Systolic blood pressure. DBP= Diastolic blood pressure.

**Table 7:** contraindication of fibrinolytic agents

### **Integrated reperfusion strategy:**

Percutaneous coronary intervention play important role in management of STEMI. Cardiac

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catheterization and coronary angiography should be carried after fibrinolytic therapy, if there are evidences of: (1) failure of reperfusion (persistent chest pain and ST-segment elevation > 90 minute) in which case a rescue Percutaneous coronary intervention is considered, (2) coronary artery reocclusion(re-elevation of ST-segment and recurrent chest pain), (3) development of recurrent ischemia or positive exercise stress test in which case an urgent percutaneous coronary interventions is considered. Routine angiography and elective percutaneous coronary interventions in asymptomatic patients following administration of fibrinolytic therapy are used with less frequency. Coronary artery bypass surgery is considered in patients, whose coronary anatomy is not suitable to percutaneous coronary intervention.

### **Hospital phase management:**

Patients should be admitted in coronary care units with continuous monitoring of the cardiac rhythm and hemodynamic monitoring. If the symptoms are controlled with oral therapy, the patients may be transferred out from coronary care unit. Patients with confirmed STEMI, who are considered to be low risk (no prior infarction, no persistent chest discomfort, congestive heart failure, hypotension and cardiac arrhythmia), may be safely transferred out of coronary care unit within 24 hours.

**Activity:** patients with STEMI should be kept at bed rest for first 6-12 hours because factors that increase the work of heart may increase the size of infarct. However in absence of complications, may advice to upright posture by dangling their feet over side of bed and sitting in chairs within 24 hours. In absence of complications and hypotension, on seconds or thirds day, patients are ambulating in their room. By 3 days after infarctions, patients should be increased their ambulation progressively.

**Diets:** patients with STEMI should receive only clear fluids or nothing by mouth for first 12 hours because there is a chance of nausea, vomiting and aspiration. Give food with rich in potassium, magnesium, fibre and low in sodium.

**Bowel management:** STEMI patients are usually suffer from constipations, so give stool softeners such as sodium sulfosuccinate 200 mg daily. If still constipation is present then prescribe laxative. Advise him to take diet rich in bulk and more water should be talk.

**Sedation:** Diazepam 5 mg or lorazepam 0.5-2 mg three to four times a day is given for sedations.

### **Pharmacology therapy:**

#### **Antithrombotic agents:**

Antiplatelet and anticoagulation therapy during the initial phase of ST-segment elevation myocardial infarction play important role. The main goal of treatment with antiplatelet and anticoagulant is to maintain the patency of infracted related coronary artery and reduce the patient's tendency to thrombosis formation. Aspirin is standard antiplatelet agents for patients with STEMI. Inhibitor of the P2Y<sub>12</sub> ADP receptors prevents activation and aggregations of platelets. The additions of P2Y<sub>12</sub> inhibitors clopidogrel with aspirin to STEMI patients reduces the risk of clinical events(death, stroke and reinfarction) and in patients receiving thrombolytic therapy has shown to prevents reocclusion of successfully reperfused infarct artery. New P2Y<sub>12</sub>

ADP receptor antagonist such as prasugrel and ticagrelor are more effective than clopidogrel in preventing ischemic complications in patients with STEMI, undergoing PCI but associated with increased risk of bleeding. Glycoprotein IIb/IIIa receptors inhibitors prevents the thrombotic complications in patients with ST-segment elevation myocardial infarction in patient who undergoing percutaneous coronary intervention.

The standards anticoagulant used is unfractionated heparin (UFH). UFH is added with aspirin and non-fibrin-specific Thrombolysis agents such as streptokinase have beneficial effect on mortality. Immediate intravenous administration of unfractionated heparin with aspirin and fibrin specific fibrinolytic agents' help in maintain the patency of infarcted related coronary artery. The recommended dose of UFH is bolus of 60 U/kg, followed by an initial infusion of 12 U/kg per hour. The activated partial thromboplastins time during maintenance therapy should be 1.5-2 time the control. Alternative to UFH for anticoagulation of patients with STEMI are low molecular weight heparin (LMWH). The advantage of LMWH is high bioavailability permitting administering subcutaneously, reliable anticoagulation without monitoring and greater antiXa: IIa activity. Enoxaparin reduces significantly composite end point of death/nonfatal reinfarction and nonfatal reinfarction/urgent revascularization compared with UFH in STEMI patients who receive fibrinolysis. Treatment with Enoxaparin is associated with high risk of bleeding. The patients with anterior location of infarction, severe left ventricular dysfunction, heart failure, history of embolism, echocardiography show the evidence of mural thrombus and atrial fibrillation are at increased risk of systemic of pulmonary thromboembolism, such patient receives full therapeutic level of anticoagulant therapy while hospitalized followed by at least 3 month of warfarin therapy.

### **Beta-blockers:**

Beta-blockers improve the myocardial oxygen demands, decrease infarct size, decrease the incidence of life threatening ventricular arrhythmia and decrease the pain. The beta-blockers are very useful for most patients in treatment of STSEMI. In the following condition with heart failure, several compromised left ventricular function, heart block, bronchial asthma, chronic obstructive pulmonary disease and orthostatic hypotension, the beta blockers are contraindicated. The beta blockers will increase the mortality in patients with heart failure, systolic BP less than 120 mm Hg and heart rates less than 60 beat/minute. We can use Cardio selective beta-blockers (metoprolol).

### **Angiotensin converting enzyme inhibitors (ACE inhibitors):**

ACE inhibitors will reduces the mortality rate after STEMI and benefits are additive who is taking with aspirin and beta blockers. The maximum benefits of ACE Inhibitors are in those patients, who have an anterior infarction, prior infarction, older patients and depressed left ventricular functions. The short term benefits occurs when ACE inhibitors prescribed to all hemodynamic stable patients with STEMI that is those with systolic BP is greater than 100 mm of Hg. The main mechanism of ACE Inhibitors involves the reduction in ventricular remodeling after infarction and subsequent reduction in risk of development of congestive cardiac failure. The rate of recurrent infarction may also be lower in patients with STEMI, who is taking ACE Inhibitors chronically after infarction. The ACE inhibitors should be continued in all patients who have

clinically evident of congestive heart failure and who have reduction in left ventricular function or regional wall motion abnormality or those who are hypertensive. The Angiotensin receptors blockers should be prescribed to STEMI patient who cannot tolerate ACE inhibitors and whose have sign of congestive heart failure.

Aldosterone blockade should be prescribed for STEMI patients without significant renal dysfunction or Hyperkalemia who are already receiving therapeutic dose of ACE inhibitors, have left ventricular ejection fraction less than 40 %, symptomatic heart failure or diabetes mellitus patients.

### **Complication and management:**

**Ventricular arrhythmia:** Isolated ventricular premature beat occurs most commonly and which is precipitated by congestive heart failure, acidosis, hypoxemia, Hypokalemia, hypo magnesium and drugs. Beta blocker is the drugs of choice for ventricular ectopic beat.

**Ventricular tachycardia:** Most commonly seen. If hemodynamically unstable perform immediate electric counter shock. If hemodynamic stable then give intravenous Amiodarone 150 mg bolus then give 1 mg/min for 6 hours than 0.5 mg per minute.

**Ventricular fibrillation:** Ventricular fibrillation occurs in 8-10% of patients who reach hospital and VT is the major cause of death who dies before receiving medical treatment. Defibrillation will restore normal sinus rhythm. The prognosis of patients with early VT is not good. If unsuccessful then initiates cardiopulmonary resuscitations. Ventricular arrhythmia that appear after few days or weeks after myocardial infarctions may lead to pump failure and may need implantation of a cardioverter defibrillator.

**Supraventricular arrhythmia:** Sinus tachycardia most commonly seen and mainly due heart failure, pain, fever, pericarditis, drugs, hypovolemia and hypoxemia. So find out the causes and treat the cause. If no cause is identified then give beta blockers, which is beneficial to reduce myocardial oxygen demand. Other Supraventricular arrhythmia such as paroxysmal Supraventricular tachycardia, atrial flutter and atrial fibrillations are mostly secondary to heart failure. So if there is hemodynamic unstable then give electrical cardioversion. In absence of heart failure, give beta blockers, verapamil or diltiazem.

### **Atrial fibrillation:**

Atrial fibrillation is the common complication and usually does not require emergency treatment. If the arrhythmia causes a rapid ventricular rate with hypotension or circulatory collapse, prompt cardioversion by immediate synchronized DC shock is essential. In stable patients digoxin or a  $\beta$ -blocker is the treatment of choice. Atrial fibrillation is often a feature of left ventricular failure. Anticoagulation is required if atrial fibrillation persists.

**Brady arrhythmias and atrioventricular blocks:** In inferior wall myocardial infarction, usually represent with bradycardia due to atrioventricular nodal ischemia. If hemodynamic compromised (hypotension, congestive heart failure, and emergences of ventricular arrhythmia) then give intravenous atropine. If no response then external temporary pacemaker implantation should be considered. In anterior wall myocardial infarction, atrioventricular conduction defect indicates extensive tissue necrosis then considered temporary

external pacemakers implantations. Indication of temporary pacemaker's implantation in myocardial infarction is listed in table 8.

---

Following are the common indication of pacemaker implantation in myocardial infarction

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1. Complete heart blocks
2. Mobitz type II heart block
3. Brady arrhythmias associated with hypotension or congestive heart failure
4. New bifasicular block
  - LBBB, RBBB+ left anterior hemi block
  - RBBB+ left posterior hemi block

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LBBB= Left bundle branch block. RBBB= Right bundle branch block.

**Table 8:** indication of pacemaker implantation in myocardial infarction

### **Ischemia:**

Patients who develop recurrent chest pain at rest or on minimal exertion following an acute coronary syndrome are at high risk and advice for coronary angiography with a view to revascularization. Patients with dynamic ECG changes and ongoing chest pain are treated with intravenous glycoprotein IIb/IIIa receptor antagonists. Patients with resistant pain or marked hemodynamic changes should be advice for emergency coronary revascularization. After Myocardial infarction, angina occurs in up to 60% of patients treated with Thrombolysis. Most patients have a residual stenosis in the infarct-related vessel which cause angina if there is still viable myocardium downstream. So all patient who have received successful Thrombolysis should be considered for early coronary angiography with a view to coronary revascularization.

### **Heart failure:**

Acute heart failure indicates extensive myocardial damage and having a bad prognosis. All most all others complications of MI are occur when acute heart failure is present. Shock in acute myocardial infarction is mostly due to left ventricular dysfunction, less commonly also due to infarction of right ventricle and sometime due to mechanical complication such as cardiac tamponade, ventricular septal defect, and acute mitral regurgitation. Several myocardial systolic dysfunction causes fall in cardiac output, systolic blood pressure and coronary perfusion pressure. Diastolic dysfunction causes rises in left ventricular end-diastolic pressure, pulmonary congestion, pulmonary edema which lead to hypoxemia that worse myocardial ischemia. Hypotension, oliguria, confusion and cold peripheries are feature of low cardiac output whereas breathlessness; hypoxemia, cyanosis and inspiratory crackles as the base of lungs are feature of pulmonary edema. Initial treatment includes diuretics (intravenous Furosemide 20 mg), inhalation of oxygen and vasodilators unless systolic blood pressure will be less than 100 mm of Hg.

### **Pericarditis:**

Acute pericarditis is common on the second and third days of myocardial infarction. The patient has Pleuritic chest pain has developed, same site which is worse on inspiration. A pericardial rub may be audible. Opiate analgesia should be used. Non-steroidal and steroidal anti-inflammatory drugs may increase the risk of aneurysm formation and myocardial rupture in the early recovery period so avoided in early stage.

The post-MI syndrome (Dressler's syndrome) is characterized by persistent fever, pericarditis and pleurisy, and is due to autoimmunity. The symptoms occur in a few weeks or even months after the infarct and subside after a few days; prolonged or severe symptoms require treatment with high-dose aspirin, NSAIDs or even corticosteroids.

### **Mechanical complication:**

- ❖ Rupture of the papillary muscle lead to pulmonary edema and shock due to the sudden onset of mitral regurgitation, which presents with a Pan systolic murmur and third heart sound. In the presence of severe valvular regurgitation, the murmur may be quiet or absent. The diagnosis is confirmed by echocardiography and emergency mitral valve replacement may be necessary.
- ❖ Rupture of the interventricular septum causes left-to-right shunting of blood through a ventricular septal defect. This presents with sudden hemodynamic deterioration accompanied by a new loud Pan systolic murmur radiating to the right sternal border. However, patients with an acquired ventricular septal defect tend to develop right heart failure rather than pulmonary edema. Doppler echocardiography and right heart catheterizations will confirm the diagnosis.
- ❖ Rupture of the ventricle may lead to cardiac tamponade and is usually fatal, although it may rarely be possible to support a patient with an incomplete rupture until emergency surgery is performed.

### **Lifestyle and risk factor modification:**

Smoking cessation: Advise him to avoid smoking.

**Hyperlipidemia:** Advice to take HMG CoA reductase enzyme inhibitors(statin 80 mg daily), reduce the level of total cholesterol, LDL level and reduce the risk of death, re-infarction, stroke. So all patients receive statin therapy after acute coronary syndrome.

**Other risk factors:** Maintain ideal body weight. Advice to taking regular exercise. Control blood glucose level and blood pressure.

### **Mobilization and rehabilitation:**

The necrotic muscle will take 5 weeks to replace with fibrous tissue so during this periods advice to restrict physical activity. When there is no any complication then patient can mobilize on second's days, discharge the patients on 5 days with gradual increase the activity with returning to work at 6 weeks.

### **Secondary prevention drug therapy:**

**Aspirin and clopidogrel:** Low dose Aspirin (75 mg) reduce the attack of infarction so continue for whole life, if there is no unwanted effect. Clopidogrel should give in combination with aspirin for three month. If the

patient can't tolerate Aspirin then clopidogrel should be given in alternative.

**Beta-blockers:** oral beta blockers (metoprolol 50 mg) reduce the long term mortality in acute myocardial infarction so low dose oral beta blockers continue for lifelong unless there is a contraindication. Minority of patients can't tolerate beta blockers because of bronchial asthma, COPD, Bradycardia, atrioventricular block and hypotension.

**Angiotensin converting enzyme inhibitors (ACE Inhibitors):** ACE inhibitors (Enalapril 10 mg BD or Ramipril 2.5-5 mg BD) prevent ventricular remodeling, prevent onset of heart failure, reduce recurrent MI, improve survival and reduce the hospitalization. If the LVEF is  $\leq 40\%$  ACE Inhibitors are ARB definitely used. So considered in all patients with acute coronary syndrome. If the patients can't tolerate ACE Inhibitors then give Angiotensin receptor blockers (valsartan 40 mg twice daily or Candesartan 4 mg daily). A patient with Acute MI and left ventricular ejection fraction is less than 35 % and either pulmonary edema or diabetes mellitus have additional benefit with mineralocorticoids receptor antagonism (eplerenone 50 mg daily).

### **Coronary revascularisation:**

Most of the low risk patients stabilize with the oral Aspirin, Clopidogrel, and anticoagulation and antianginal drug therapy and mobilized rapidly. In low risk patients and in patient with no recurrent symptom have no benefit from routine coronary angiography. Coronary artery angiography considered in patient with moderate to high risk patients, who have fail to medical therapy, recurrent symptom, extensive ECG change, elevated Troponin level in plasma and those with pre-existing stable angina.

### **Device Therapy:**

Implantable cardiac defibrillators (ICD) will prevents sudden cardiac death in patients who have impairment of left ventricular function (LVEF  $\leq 30\%$ ) after myocardial infarction.

### **Prognosis:**

All most one-fourth of all case of myocardial infarction death occurs within minute to hour without medical care. Half of death occurs within 24 hour of onset of symptom and 40 % of all affected patients will dies within first month. The prognosis will be better who reach the hospital within one hour of onset of symptom. Early death is mostly due to arrhythmia. Outcome depends on extent of myocardial damage and unfavorable feature includes poor left ventricular function, Atrioventricular block and life threatening persistent ventricular arrhythmia. The prognosis is worse for anterior than inferior infarcts. Bundle branch block, high cardiac markers level and dynamic ECG change indicates extensive myocardial damage and having poor prognosis. Old age, depression patient and social isolation patient also have poor prognosis.

### **Literature Review:**

Slow blood flow or no reflow blood phenomena is defined as no blood flow or slow blood flow in infarcted related coronary artery after percutaneous coronary intervention( Stenting or balloon inflation), without angiographic evidences of mechanical vessel obstruction, resulting in no perfusion or hypoperfusion in myocardium<sup>[1, 4, 5, 7, 8]</sup>. Slow blood flow or no reflow phenomenon is associated with poor left ventricular

functions recovery and worse long term outcomes. The exact mechanism of slow blood flow or no reflow phenomenon after PCI is not established till now. Slow blood flow after percutaneous coronary intervention is a series complication in the treatment of ST-Elevation myocardial infarction, unstable angina and coronary total occlusion [5, 9, 10]. The no reflow phenomenon after PCI is strong predictors of death extending up to 5 years, in patients with STEMI [11].

### **Risk factors of slow blood flow or no reflow phenomenon:**

The patient with slow blood flow or no reflow phenomenon in infarcted related blood vessel after emergency PCI in STEMI is related to genetically susceptibility and diabetes mellitus, smoking, Hypertension, Hyperlipidemia are unfavorable conditions for no reflow phenomenon as shown in table 9[12-14]. The inflammatory markers such as C-reactive protein (CRP) and interleukin-6(IL-6) also play major role in restenosis after PCI [15-18]. Other risk factors included high WBC count, thrombus grade, pain duration, maximal ST-changes, Left ventricular function, bifurcation and coronary anatomy. Incidences are higher in patients with high thromboembolic lesions [19, 20]. There is also relationship between the onset time of acute myocardial infarction and slow blood flow phenomenon during surgery. The longer the onset of acute MI, there is a higher incidence slow blood flow or no reflow phenomenon.

---

Following are the risk factors of slow blood flow after PCI in patients with STEMI

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1. Smoking
  2. Diabetes mellitus
  3. Age
  4. Systolic Blood pressure
  5. Local interleukin
  6. Hyperlipidemia
  7. Increased white blood cells count
  8. Pain duration
  9. Coronary anatomy
  10. LV function
- 

PCI: Percutaneous coronary intervention. STEMI: ST-Segment elevation myocardial infarction. LV: Left ventricular.

**Table 9:** Risk factors of slow blood flow after PCI in patients with STEMI [1, 13, 14]

### **Mechanism of slow blood flow or no reflow phenomenon:**

The exact mechanism of slow blood flow or no reflow phenomenon is not understood but the main mechanism considered is myocardial ischemic injury, endothelial dysfunction, microvascular spasm, microvascular dysfunction, myocardial reperfusion injury, distal coronary artery embolization and microcirculation injury [1, 5, 13, 21, 22]. Myocardial ischemia causes damage to vascular endothelium, adhesion of

platelets and Neutrophil causes occlusion of the lumen, which aggravating microcirculatory disorders. After the myocardial reperfusion, there is increased production of oxygen free radical, calcium overload, and infiltration of acute inflammatory cells such as Neutrophil and activation of apoptotic signaling pathways, which aggravate ischemia [23, 24]. Acute myocardial infarction patients undergo PCI, due to balloon expansion or stent implantation, intracoronary plaques rupture micro particles which lead to vascular obstruction in distal coronary artery [5]. When the diameter of particles is less than 200  $\mu\text{m}$ , which generally does not causes vascular obstruction and when the diameter of the particle is greater 200  $\mu\text{m}$ , which causes severe microvascular obstruction. The thromboxane or Angiotensin released by plaques, which may lead to microcirculatory disorders [21, 25, 26]. The culprit lesion in STEMI are composed of fragile tissue such as cholesterol, foam cells, thrombus and micro calcification [27], which causes distal embolization following stent implantation, resulting slow blood flow [28].

The shorter the pain duration, fresh clot in artery and fresh clot increase the occurrences of no-reflow phenomenon in acute MI patients after PCI [29-31]. The high WBC counts will increase inflammation and aggregation of WBC in artery of myocardium, which causes no-reflow phenomenon [32]. The increased clot volume causes higher thrombus grade, which increased the possibility of no-reflow phenomenon [33]. So WBC counts and thrombus grade are most important predictive factors of developing no-reflow phenomenon [30, 32]. The number of abnormal pathological Q-waves, larger infarct size and wall motion score are also most important predictive factors for developing no-reflow phenomenon [8, 11].

The cytokines, interleukin-6(IL-6) is implicated in both proinflammatory and anti-inflammatory response in development of slow flow or no-reflow phenomenon [34]. In chronic inflammatory condition such as idiopathic pulmonary fibrosis, bronchial asthma, arthritis, colitis, IL-6 play a proinflammatory role while in acute inflammation, its play role as anti-inflammatory [35]. The inflammatory markers such as C-reactive protein and IL-6 play important role in occurrences of restenosis after PCI [15-18, 36]. So the elevation of IL-6 is important indicators of increased mortality rate in case of ST-Segment elevation of myocardial infarction, who undergoes PCI [36, 37].

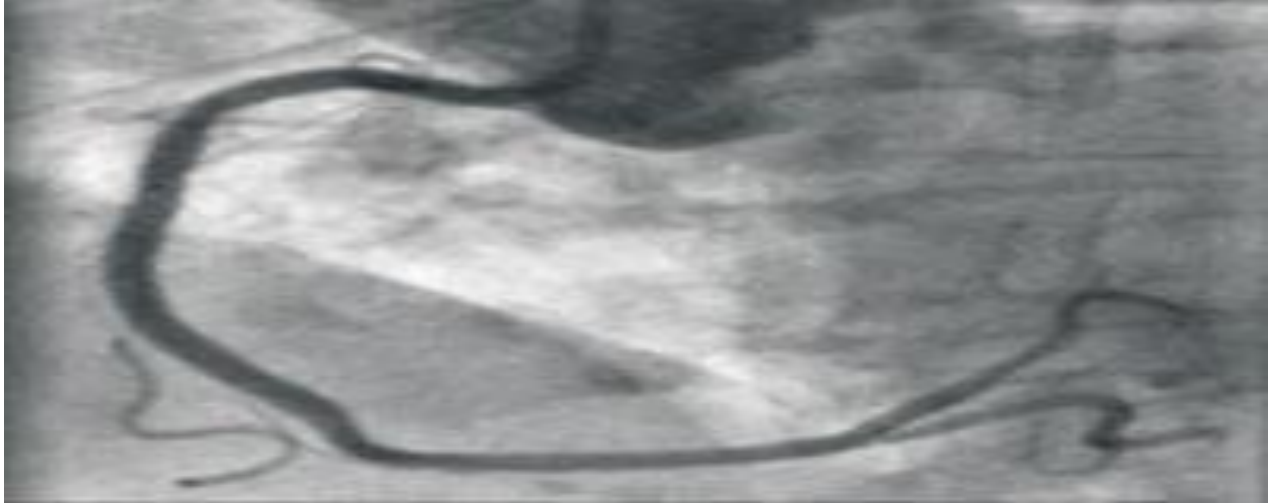
In patients with percutaneous coronary intervention at greater than 3 hours onset of acute MI, having white thrombus are more likely to have no-reflow or slow blood flow after stent implantation than patients with red thrombus. This will predicts, there is a slow blood flow or re-flow phenomenon after stent implantation.

### **Management of slow blood flow or no-reflow phenomenon after percutaneous coronary intervention:**

In patients with hyper thrombotic lesions, to achieve complete recanalization of infarcted coronary artery, pre-coronary administration of drugs such as glycoprotein IIb/IIIa receptors antagonist can be given for prevention of slow blood flow after PCI.

Medical treatment with sodium nitropruside [38], Nicorandil [39] nitroglycerin, Diltiazem and verapamil [38, 40] are effective in relaxing vascular smooth muscle, regulated endothelial function and

preventing microvascular spasm as shown in table 10 [1, 38] and figure 1. These medicines lowered the blood pressure, among which verapamil and diltiazem causes malignant Atrioventricular blocks and significant bradycardia while nitropruside and nitroglycerin causes increase heart rate [1]. Therefore the effectiveness for the intravenous infusion of these drugs after PCI is still controversial.



**Figure 1:** show slow blood flow improved after intracoronary injection of verapamil and nitroglycerin

Prostaglandin E1 (PGE1) is widely used now a day in clinical practices due to its beneficial effects on fibrinolysis, vasodilatation and platelet disaggregation [1]. Alprostadil is a kind of liposomal PGE1, which dilates the coronary arterioles [1] and prevent coronary restenosis [1]. Alprostadil accumulates around the target lesion, which lead to mild cardiopulmonary side effects but Alprostadil will dilate the coronary arteries and improve the coronary circulation in STEMI is still controversial.

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Following are the drugs used for prevention of slow blood flow after PCI in STEMI

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1. Verapamil
  2. Diltiazem
  3. Nitroglycerin
  4. Sodium nitropruside
  5. Alprostadil
  6. Nicorandil
- 

**Table 10:** Drugs used for prevention of slow blood flow after PCI in patients with STEMI [1, 38]

Mechanical technique such as thrombus aspiration and distal protection devices can be chosen to tackle thrombus in major coronaries arteries [1]. An intracoronary drugs infusion technique is more commonly used for small vessel where thrombus is not visible [1]. Thrombus aspiration during primary percutaneous coronary intervention show controversial result for the effectiveness of aspiration of thrombus [41-43].

A slow blood flow or no-reflow phenomenon is one of the major and common complications in STEMI, who undergoes percutaneous coronary intervention. The incidences of slow blood flow phenomenon

is ranges from 5 % to 25 % [1]. The no-reflow phenomenon, if not reversed, then causes high mortality and morbidity rate [44].

Slow blood flow or no re-flow phenomenon is strong predictors of major cardiac complications such as congestive heart failures, life threatening malignant arrhythmia [45, 46] and cardiac death after PCI in patients with STEMI thus induces higher in hospital mortality and poor long term prognosis [47].

### **Aims and Objectives Of the Study:**

Aim of this study is to compare the different mode of administration of sodium nitropruside that is distal micocather infusion and intracoronary infusion before the stent implantation during percutaneous coronary intervention to prevent the slow blood flow in treatment of ST-segment elevation myocardial infarction. We will make comparison in TIMI blood flow, left ventricular ejection fraction, systolic blood pressure, dyspnea grading on the basis of NYHA, Age, sex, pulse rate and symptomatic parameters which can help us to choose perfect technique to be applied in future. We will compare the effects of sodium nitropruside in these two methods in our hospital.

### **Objective of the study is:**

To compare the distal micocather infusion and intracoronary infusion of sodium nitropruside before the stent implantation in PCI to prevent the slow flow of blood flow during treatment of STEMI.

Our prospective study will give insight about the better administration of sodium nitropruside and help us to know the effects of this different mode of administration.

### **Key Points:**

There were limited studies that were directly comparing the distal micocather infusion and intracoronary administration. Due to its vast nature many researches were limited to certain parameters in each study. There were plenty of researches that showing comparison in each group after certain period of time.

- ❖ Our study is single centered prospective study with the limited period of around 12 months, our findings may be clinically significant and reliable only for our hospital setup, which may or may not be true for another hospital or center setup.
- ❖ Our study data were collected at the interval of 12 months before and after the hospital, so it was easier to collect data when patients were admitted in hospital before the procedure but it was somewhat difficult to collect them at 12-month interval because they were followed up at OPD setting and chances of missing important data was high. My professor helped me during collection of data during this study.

### **Research Study Plan:**

For research topic I consulted with my Professor and we finally selected the topic Comparison of distal micocather infusion and intracoronary administration of sodium nitropruside before the implantation during percutaneous coronary intervention to prevent slow flow of blood during treatment of ST-segment

elevation myocardial infarction. Intracoronary administration of sodium nitropruside was performed in our hospital for a long time but distal micocather infusion was started recently. So, we decided to conduct a thesis comparing these techniques. We selected few variables which are feasible to collect at inpatient and outpatient setting, routinely performed and good indicator for the comparing the administration technique. Reference lists of included studies, relevant articles and systemic reviews were assessed. Search engines like Google, Bing, and PubMed were used to search other researches and words like distal micocather infusion and intracoronary administration were used. Proposal was submitted to the university and ethical approvals were taken from the hospital and the University for Commencement of the study. Data were collected once at the time of admission before the procedure and one more time at the routine follow-up at the interval of 3 months. Data collection duration was 12 months. After analyzing the data, thesis was prepared and submitted.

## MATERIAL AND METHODS

### Study Design:

The prospective observational study was done on the patients that were evaluated, admitted and planned for percutaneous coronary interventions at the department of cardiology in the First People's Hospital of Jingzhou (First affiliated clinical hospital of Yangtze University). Patients were extensively evaluated with repetitive ECGs and angiography for identification of the underlying illness and indication for the percutaneous coronary intervention usually during earlier visits and admissions. This prospective study was conducted from November 2018 to November 2019. Data were collected before the procedure, some immediately after the procedure and most of them again at the follow-up at 3 months. Our study focused on the slow blood phenomenon after administration of sodium nitropruside function after the patient going percutaneous coronary intervention. We carried out our study on two groups; i) distal micocather infusion of sodium nitropruside and ii) intracoronary administration of sodium nitropruside. Indication of percutaneous coronary interventions is acute ST-segment elevation myocardial infarctions and selection of implantation was randomly selected between these two methods. Baseline variables data were collected when patient were at the inpatient department of the hospital for the implantation and follow-up data were mostly collected at the OPD. Baseline variables were collected from the patients undergoing PCI and follow-up data were collected. Variables that we included in our study are measured or performed routinely for these methods.

Study Location: Department of Cardiology, The First People's Hospital of Jingzhou  
(First affiliated clinical hospital of Yangtze University), Shashi, Jingzhou, Hubei, China

**Study Period:** November 2018– November 2019.

**Study Design:** Prospective observational study.

## **Study Methodology:**

### **Source of samples:**

Patients underwent percutaneous coronary intervention with distal micocather infusion of sodium nitropruside and intracoronary administration of sodium nitropruside to prevent slow blood flow at the department of cardiology, the first people's hospital of Jingzhou from November 2018 and November 2019.

### **Patient selection:**

Patients were thoroughly examined in course of time and indicated for percutaneous coronary intervention. Primary indication for PCI is ST-segment elevation myocardial infarction. Patients having either distal micocather infusion or intracoronary administration of sodium nitropruside and are on regular follow-up. Patients were fully notified with all the procedural indications and complications before the implantation and consent for using their laboratory, clinical and procedural variables were also taken at the same time. Study consent contained that we will be using laboratory, clinical and procedural variables for research purpose and no use of personal identifiable information in the study. Patient kept on observation for few days and then discharged.

### **Inclusion Criteria:**

Patients who underwent percutaneous coronary intervention i.e. either distal micocather infusion of sodium nitropruside or intracoronary administration of sodium nitropruside before the stent implantation to prevent of slow blood flow phenomena.

- ❖ •Patient with successful percutaneous coronary infusion with nitropruside infusion.
- ❖ •Patients with regular follow-up. In our study variables were assessed at 3-month follow-up.

### **Exclusion Criteria:**

- ❖ •Patient with unsuccessful implantation.
- ❖ •Patients not followed-up at 6-month interval.
- ❖ •Patients with incomplete information at 0 and 3 months.

### **Dependent (outcome) variables:**

Dependent variables we collected in our study are; LVEF, mortality, ST-segment restoration, TIMI Blood flow. .

- ❖ LVEF = Left ventricular ejection fraction was determined by echocardiography.
- ❖ ST-segment restoration through ECG.
- ❖ TIMI blood flow: through coronary artery angiography.
- ❖ Mortality: through follow up.

### **Independent (explanatory) variables:**

Independent variables that were collected: age, sex, indication, associated comorbidities.

### Statistical Analysis:

All of the collected data are entered, stored and analyzed through SPSS Statistics IBM version 24.0 software and Microsoft Excel. References and bibliography are maintained by Endnote 7. Data information is given in tabulation form and pie chart form. Categorical groups are expressed in percentage and compared using Chi-square test. Measurement of normally distributed data of variables are expressed as Mean  $\pm$  SD and calculated with help of paired t-test. *P* value of  $<.05$  was considered statistical significant.

### RESULTS

Data were collected from the patients who underwent percutaneous coronary intervention cardiology department of First People's Hospital of Jingzhou. Patient information and data were recorded before the procedure and at the 3-month interval for the comparison. Due to longer duration of follow-up all the patient who underwent percutaneous coronary intervention could not follow-up during our study period from November 2018 to November 2019. All the data were collected and recorded in spread sheet. *P* value for individual variables were calculated using paired t-test and *P* value for proportion (%) were calculated using Chi-square test.

In our study, distal micocather infusions of sodium nitropruside group consist of 30 patients and Guiding Cather infusion group consisting 30 patients. Mean age of patients are  $65 \pm 7.6$  and  $67.2 \pm 5.3$  years in group MCI and CON respectively. *P* value of age between both group is 0.39 which is statistically insignificant ( $P < 0.05$  significant). There are 70 % male in MCI group and 66.7 % in CON group. *P* value of male sex between both group is 0.93 which is statistically insignificant ( $P < 0.05$  significant). Full restoration of ST-segment rate are 93.3% in MCI group and 70.0 % in CON group respectively ( $p > 0.05$ ). Mortality rate during hospitalization are 3.3% in MCI group and 6.6% in CON group respectively ( $p > 0.05$ ). At discharge, LVEF are  $50.3\% \pm 5.4\%$  in MCI group and  $44.6\% \pm 6.0\%$  in CON group respectively. The TIMI blood flow classification between MCI group and CON group was shown in table 11 and table ( $p > 0.05$ ). The major hemorrhagic complication rate is 3.33 % in MCI group and 6.66 % in CON group ( $p > 0.05$ )

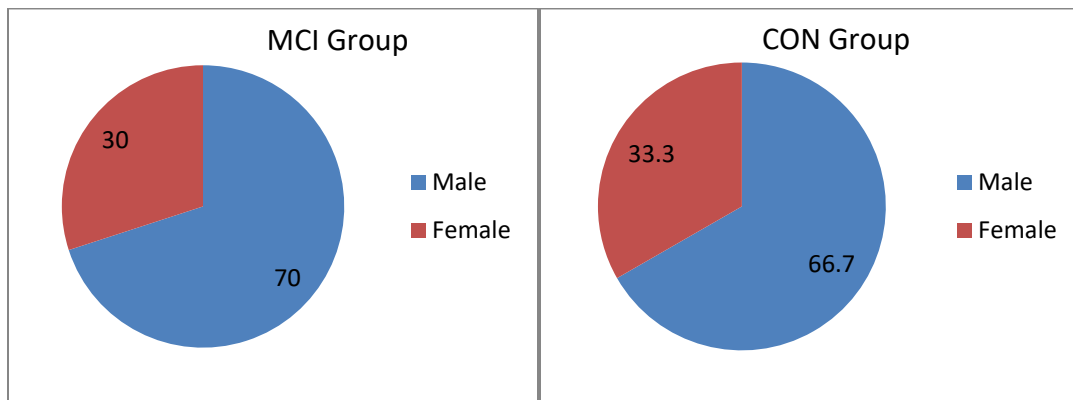
Characters	MCI Group	CON group	p value
1. Male	70 %	66.7 %	0.39
2. Age	65±7.6	67.2±5.3	0.93
3. Body weight	64.0±10.3	69.2±9.7	0.42
4. Hypertension	60.0 %	53.3 %	0.32
5. Diabetes	26.7 %	36.7 %	0.42
6. Smoking	43.3 %	30.0 %	0.31
7. ST-segment restoration	93.3%	70.0 %	0.40
8. Mortality	3.3%	6.6 %	0.92
9. LVEF	50.3%±5.4%	44.6%±6.0%	0.73
10. Hemorrhagic complication	3.33 %	6.66 %	0.40
11. IRA:			
•LAD	13	11	
•LCA	5	7	
•RCA	12	12	

LVEF: Left ventricular ejection fraction.

**Table 11:** Base line Characters.

TIMI Classification	MCI Group	CON Group
0	1	5
1	3	6
2	5	6
3	21	13

**Table 12:** The TIMI blood flow classification between MCI Group and CON group



**Figure 2:** male and female in each group

## DISCUSSION

Percutaneous coronary intervention was great invention for human health. Progress in each previous invention is an ongoing process. Percutaneous coronary is one of the great achievements in interventional cardiology. Being an easy access, PCI been widely used around the world. However, after been popular for such a long year its detrimental effects began to surface. Many studies have indicated its harmful effects and also advocated new techniques to overcome these shortcomings. Multiple studies showed not many differences in outcomes with different mode of administration of sodium nitropruside before the stent implantation during PCI. Our study focused on administration of sodium nitropruside during PCI before the stent implantation when compared with distal micocather infusion of nitropruside and intracoronary administration of sodium nitropruside. Distal micocather infusion of sodium nitropruside was, showing increasing popularity due to its positive outcomes. In our study we compared the variables of the patients those underwent distal micocather infusion and intracoronary administration of sodium nitropruside. Follow-up time for compare was 3 months. The purpose of keeping 3-month duration was most of the detrimental or improvement can't be properly seen at shorter period of time. As we were more focused on cardiac function that usually require longer time. As in other studies we also do have male dominant in our study. As our main indication of PCI is ST-segment elevation myocardial infarction permanent. Our study focused on few variables that express the functions of the heart. One of the main indicators of the cardiac function is LVEF. It is also the indicator for overall cardiac function. Our study clearly showed the increase of LVEF in MCI group and decrease in CON group. Baseline LVEF was  $57.47 \pm 7.22$  % in MCI group and it was  $50.3\% \pm 5.4\%$  in 3 months which clearly indicates good. On the other hand, there was decrease in LVEF in CON group. Studies also show better outcome in ST-segment restoration MCI group that 93.3 % restoration Of ST-segment in MCI group and 70 % restoration of ST-segment in CON groups. Studies also show that mortality rate is less in MCI group compared to CON group that is mortality rate 3.3 % in MCI group and 6.6 % in CON groups. Our studies also show that major hemorrhagic complication is very less in MCI group as compared to CON group that is complication rate is 3.33 % in MCI group and 6.66% in CON group respectively( $P > 0.05$ )

## CONCLUSION

Variables we applied in our study are very basic and routinely done and reflect over all condition of the heart. We choose our variables in different categories like echocardiography (LVEF), clinical examination, ECG (ST-segment restoration), TIMI classifications and mortality rate. We found better results in MCI group in all the variables we examined. We noted better outcome on LVEF. LVEF in CON group lowered on follow-up whereas MCI group has stable LVEF. As most of the studies suggested, our final result also directs the conclusion in the same direction. Distal micocather infusion of sodium nitropruside showed better outcomes in ventricular functions parameters. We can conclude that distal micocather infusion of sodium nitropruside has better post procedural outcomes over intracoronary administration of sodium nitropruside when compared over ventricular functions. Hemorrhagic complication rate is very less in MCI group as compared to

CON group. Slow blood flow is a common complication after percutaneous coronary intervention in patients with ST-Segment elevation myocardial infarction, unstable angina and coronary total occlusion and associated with poor outcomes. The slow blood flow or no-reflow phenomenon remains a significant challenge for STEMI and unstable angina patients. It is associated with poor prognosis. Time of acute myocardial infarction, WBC count, diabetes mellitus, and hypertension, characters of thrombus, thrombus grading, age, and ratio of stent diameters to vessel diameters are the strong predictive factors for developing slow blood flow or no-reflow phenomenon after percutaneous coronary intervention in patient with ST-segment elevation myocardial infarction.

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