A STUDY ON QT DISPERSION AND THROMBOLYTIC THERAPY IN ACUTE MYOCARDIAL INFARCTION

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CERTIFICATE

This is to certify that this dissertation entitled **"A Study on QT Dispersion and Thrombolytic therapy in Acute Myocardial Infarction"** presented herewith by **Dr.N.RAMYA** to the Faculty of Medicine, The Tamilnadu Dr M.G.R Medical University ,Chennai in partial fulfillment of the requirement for the award of the M.D Degree (Branch I) General Medicine, is a bonafide research work carried out by her under our direct supervision and guidance.

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DECLARATION

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This is submitted to the The Tamilnadu Dr M.G.R Medical University. Chennai,in partial fulfillment of the rules and regulations of the MD Degree examination in General Medicine.

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INTRODUCTION

Myocardial infarction is a common presentation of ischemic heart disease. Ischemic heart disease is the leading cause of death in developed countries, but third to AIDS and lower respiratory infections in developing countries.

In India, cardiovascular disease (CVD) is the leading cause of death. The deaths due to CVD in India were 32% of all deaths in 2007 and are expected to rise from 1.17 million in 1990 and 1.59 million in 2000 to 2.03 million in 2010. Although a relatively new epidemic in India, it has quickly become a major health issue with deaths due to CVD expected to double during 1985-2015. Mortality estimates due to CVD vary widely by state, ranging from 10% in Meghalaya to 49% in Punjab (percentage of all deaths). Punjab (49%), Goa (42%), Tamil Nadu (36%) and Andhra Pradesh (31%) have the highest CVD related mortality estimates. State-wise differences are correlated with prevalence of specific dietary risk factors in the states. Moderate physical exercise is associated with reduced incidence of CVD in India (those who exercise have less than half the

risk of those who don't). CVD also affects Indians at a younger age (in their 30s and 40s) than is typical in other countries.

QTc dispersion is an important marker that reflect variations of ventricular repolarisation and arrythmogenic potential. This study is based on various studies suggesting significant reduction in QTc dispersion after thrombolytic therapy in acute myocardial infarction.

REVIEW OF LITERATURE

MYOCARDIAL INFARCTION

Classification

There are two basic types of acute myocardial infarction, (1) transmural MI- is associated with atherosclerosis involving major coronary artery. It can be subclassified into anterior,posterior or inferior. (2) subendocardial MI- involves small area, in the subendocardial wall of the left ventricle, ventricular septum, papillary muscles.Clinically, myocardial infarction is further sub classified into ST elevation MI verses non ST elevation MI based on ECG changes.

Signs and symptoms

The onset of symptoms in myocardial infarction (MI) is usually gradual, over several minutes, and rarely instantaneous. Chest pain is the most common symptom of acute myocardial infarction and is often described as a sensation of tightness, pressure, or squeezing. Chest pain due to ischemia (a lack of blood and hence oxygen supply) of the heart muscle is termed angina pectoris. Pain radiates most often to the left arm, but may also radiate to the lower jaw, neck, right arm, back, and epigastrium, where it may mimic heartburn. Levine's sign, in which the patient localizes the chest pain by clenching their fist over the sternum, has classically been thought to be predictive of cardiac chest pain.

Shortness of breath (dyspnea) occurs when the damage to the heart limits the output of the left ventricle, causing left ventricular failure and consequent pulmonary edema. Other symptoms include diaphoresis (an excessive form of sweating), weakness, light-headedness, nausea, vomiting, and palpitations. These symptoms are likely induced by a massive surge of catecholamine's from the sympathetic nervous system, which occurs in response to pain and the hemodynamic abnormalities that result from cardiac dysfunction. Loss of consciousness (due to inadequate cerebral perfusion and cardiogenic shock) and even sudden death (frequently due to the development of ventricular fibrillation) can occur in myocardial infarctions.

Women and older patients experience atypical symptoms more frequently than their male and younger counterparts. Women also have more symptoms compared to men (2.6 on average vs. 1.8 symptoms in men). The most common symptoms of MI in women include dyspnea, weakness, and fatigue. Fatigue, sleep disturbances, and dyspnea have been reported as frequently occurring symptoms which may manifest as long as one month before the actual clinically manifested ischemic event. In women, chest pain may be less predictive of

coronary ischemia than in men. Approximately half of all MI patients have experienced warning symptoms such as chest pain prior to the infarction.

Approximately one fourth of all myocardial infarctions are silent, without chest pain or other symptoms. These cases can be discovered later on electrocardiograms or at autopsy without a prior history of related complaints. A silent course is more common in the elderly, in patients with diabetes mellitus and after heart transplantation, probably because the donor heart is not connected to nerves of the host. In diabetics, differences in pain threshold, autonomic neuropathy, and psychological factors have been cited as possible explanations for the lack of symptoms.

Any groups of symptoms compatible with a sudden interruption of the blood flow to the heart are called an **acute coronary syndrome.**

The differential diagnosis includes other catastrophic causes of chest pain, such as pulmonary embolism, aortic dissection, pericardial effusion causing cardiac tamponade, tension pneumothorax, and esophageal rupture.

Causes and risk factors

Heart attack rates are higher in association with intense exertion, be it psychological stress or physical exertion, especially if the exertion is more intense than the individual usually performs. Quantitatively, the period of intense exercise and subsequent recovery is associated with about a 6-fold higher myocardial infarction rate (compared with other more relaxed time frames) for

people who are physically very fit. For those in poor physical condition, the rate differential is over 35-fold higher. One observed mechanism for this phenomenon is the increased arterial pulse pressure stretching and relaxation of arteries with each heart beat which, as has been observed with intravascular ultrasound, increases mechanical "shear stress" on atheromas and the likelihood of plaque rupture.Acute severe infection, such as pneumonia, can trigger myocardial infarction. A more controversial link is that between *Chlamydophila pneumoniae* infection and atherosclerosis.

There is an association of an increased incidence of a heart attack in the morning hours, more specifically around 9 a.m. Some investigators theorize that this increased incidence may be related to the circadian variation in cortisol production affecting the concentrations of various cytokines and other mediators of inflammation.

Risk factors

Risk factors for atherosclerosis are generally risk factors for myocardial infarction:

- Diabetes (with or without insulin resistance) - the single most important risk factor for ischemic heart disease (IHD)
- Tobacco smoking
- Hypercholesterolemia (more accurately hyperlipoproteinemia, especially high low density lipoprotein and low high density lipoprotein)
- High blood pressure
- Family history of ischemic heart disease (IHD)
- Obesity (defined by a body mass index of more than 30 kg/m², or alternatively by waist circumference or waist-hip ratio).
- Old age
- Hyperhomocysteinemia (high homocysteine, a toxic blood amino acid that is elevated when intakes of vitamins B2, B6, B12 and folic acid are insufficient)
- Stress (occupations with high stress index are known to have susceptibility for atherosclerosis)

  Males are more at risk than females.

Women who use combined oral contraceptive pills have a modestly increased risk of myocardial infarction, especially in the presence of other risk factors, such as smoking.

Inflammation is known to be an important step in the process of atherosclerotic plaque formation. C-reactive protein (CRP) is a sensitive but non-specific marker for inflammation. Elevated CRP blood levels, especially measured with high sensitivity assays, can predict the risk of MI, as well as stroke and development of diabetes.

Inflammation in periodontal disease may be linked coronary heart disease, and since periodontitis is very common, this could have great consequences for public health.

Baldness, hair graying, a diagonal earlobe crease (Frank's sign) and possibly other skin features have been suggested as independent risk factors for MI. Their role remains controversial; a common denominator of these signs and the risk of MI is supposed, possibly genetic.

Calcium deposition is another part of atherosclerotic plaque formation. Calcium deposits in the coronary arteries can be detected with CT scans. Several studies

have shown that coronary calcium can provide predictive information beyond that of classical risk factors.

Pathophysiology

A myocardial infarction occurs when an atherosclerotic plaque slowly builds up in the inner lining of a coronary artery and then suddenly ruptures, totally occluding the artery and preventing blood flow downstream.

Acute myocardial infarction refers to two subtypes of acute coronary syndrome, namely **non-ST-elevated myocardial infarction** and **ST-elevated myocardial infarction**, which are most frequently (but not always) a manifestation of coronary artery disease. The most common triggering event is the disruption of

an atherosclerotic plaque in an epicardial coronary artery, which leads to a clotting cascade, sometimes resulting in total occlusion of the artery. Atherosclerosis is the gradual buildup of cholesterol and fibrous tissue in plaques in the wall of arteries (in this case, the coronary arteries), typically over decades. Blood stream column irregularities visible on angiography reflect artery lumen narrowing as a result of decades of advancing atherosclerosis. Plaques can become unstable, rupture, and additionally promote a thrombus (blood clot) that occludes the artery; this can occur in minutes. When a severe enough plaque rupture occurs in the

coronary vasculature, it leads to myocardial infarction (necrosis of downstream myocardium).

If impaired blood flow to the heart lasts long enough, it triggers a process called the ischemic cascade; the heart cells in the territory of the occluded coronary artery die (chiefly through necrosis) and do not grow back. A collagen scar forms in its place. Recent studies indicate that another form of cell death called apoptosis also plays a role in the process of tissue damage subsequent to myocardial infarction. As a result, the patient's heart will be permanently damaged. Myocardial scarring also puts the patient at risk for potentially life threatening arrhythmias, and may result in the formation of a ventricular aneurysm that can rupture with catastrophic consequences.

Injured heart tissue conducts electrical impulses more slowly than normal heart tissue. The difference in conduction velocity between injured and uninjured tissue can trigger re-entry or a feedback loop that is believed to be the cause of many lethal arrhythmias. The most serious of these arrhythmias is ventricular fibrillation, an extremely fast and chaotic heart rhythm that is the leading cause of sudden cardiac death. Another life threatening arrhythmia is ventricular tachycardia , which may or may not cause sudden cardiac death. However, ventricular

tachycardia usually results in rapid heart rates that prevent the heart from pumping blood effectively. Cardiac output and blood pressure may fall to dangerous levels, which can lead to further coronary ischemia and extension of the infarct.

The cardiac defibrillator is a device that was specifically designed to terminate these potentially fatal arrhythmias. The device works by delivering an electrical shock to the patient in order to depolarize a critical mass of the heart muscle, in effect "rebooting" the heart. This therapy is time dependent, and the odds of successful defibrillation decline rapidly after the onset of cardiopulmonary arrest.

Diagnosis

The diagnosis of myocardial infarction is made by integrating the history of the presenting illness and physical examination with electrocardiogram findings and cardiac markers (blood tests for heart muscle cell damage).A coronary angiogram allows visualization of narrowing's or obstructions on the heart vessels, and therapeutic measures can follow immediately

A chest radiograph and routine blood tests may indicate complications or precipitating causes and are often performed upon arrival to an emergency department. New regional wall motion abnormalities on an echocardiogram are also suggestive of a myocardial infarction. Echo may be performed in equivocal cases by the on-call cardiologist.[citation needed] In stable patients whose symptoms have resolved by the time of evaluation,technetium-99m 2-methoxyisobutylisonitrile (Tc99m MIBI) or thallium-201 chloride can be used in nuclear medicine to visualize areas of reduced blood flow in conjunction with physiologic or pharmacologic stress. Thallium may also be used to determine viability of tissue, distinguishing whether non-functional myocardium is actually dead or merely in a state of hibernation or of being stunned.

Diagnostic criteria

WHO criteria have classically been used to diagnose MI; a patient is diagnosed with myocardial infarction if two (probable) or three (definite) of the following criteria are satisfied:

1. Clinical history of ischaemic type chest pain lasting for more than 20 minutes
2. Changes in serial ECG tracings
3. Rise and fall of serum cardiac biomarkers such as creatine kinase-MB fraction and troponin

The WHO criteria were refined in 2000 to give more prominence to cardiac biomarkers. According to the new guidelines, a cardiac troponin rise accompanied by either typical symptoms, pathological Q waves, ST elevation or depression or coronary intervention are diagnostic of MI.

Physical examination

The general appearance of patients may vary according to the experienced symptoms; the patient may be comfortable, or restless and in severe distress with an increased respiratory rate. A cool and pale skin is common and points to vasoconstriction. Some patients have low-grade fever (38–39 °C). Blood pressure may be elevated or decreased, and the pulse can be become irregular.

If heart failure ensues, elevated jugular venous pressure and hepatojugular reflux, or swelling of the legs due to peripheral edema may be found on inspection.

Rarely, a cardiac bulge with a pace different from the pulse rhythm can be felt on precordial examination. Various abnormalities can be found on auscultation, such as a third and fourth heart sound, systolic murmurs, paradoxical splitting of the second heart sound, a pericardial friction rub and rales over the lung.

Electrocardiogram

The primary purpose of the electrocardiogram is to detect ischemia or acute coronary injury in broad, symptomatic emergency department populations. However, the standard 12 lead ECG has several limitations. An ECG represents a brief sample in time. Because unstable ischemic syndromes have rapidly changing supply versus demand characteristics, a single ECG may not accurately represent the entire picture. It is therefore desirable to obtain *serial* 12 lead ECGs, particularly if the first ECG is obtained during a pain-free episode. Alternatively, many emergency departments and chest pain centers use computers capable of continuous ST segment monitoring. The standard 12 lead ECG also does not directly examine the right ventricle, and is relatively poor at examining the posterior basal and lateral walls of the left ventricle. In particular, acute myocardial infarction in the distribution of the circumflex artery is likely to produce a nondiagnostic ECG. The use of additional ECG leads like right-sided leads V3R

and V4R and posterior leads V7, V8, and V9 may improve sensitivity for right ventricular and posterior myocardial infarction. In spite of these limitations, the 12 lead ECG stands at the center of risk stratification for the patient with suspected acute myocardial infarction. Mistakes in interpretation are relatively common, and the failure to identify high risk features has a negative effect on the quality of patient care.

The 12 lead ECG is used to classify patients into one of three groups:

1. those with ST segment elevation or new bundle branch block (suspicious for acute injury and a possible candidate for acute reperfusion therapy with thrombolytics or primary PCI),
2. those with ST segment depression or T wave inversion (suspicious for ischemia), and
3. those with a so-called non-diagnostic or normal ECG.

A normal ECG does not rule out acute myocardial infarction. Sometimes the earliest presentation of acute myocardial infarction is the hyperacute T wave, which is treated the same as ST segment elevation. In practice this is rarely seen, because it only exists for 2–30 minutes after the onset of infarction. Hyperacute T waves need to be distinguished from the peaked T waves associated with hyperkalemia. The current guidelines for the ECG diagnosis of acute myocardial

infarction require at least 1 mm (0.1 mV) of ST segment elevation in the limb leads, and at least 2 mm elevation in the precordial leads. These elevations must be present in anatomically contiguous leads. (I, aVL, V5, V6 correspond to the lateral wall; V1-V4 correspond to the anterior wall; II, III, aVF correspond to the inferior wall.) This criterion is problematic, however, as acute myocardial infarction is not the most common cause of ST segment elevation in chest pain patients. Over 90% of healthy men have at least 1 mm (0.1 mV) of ST segment elevation in at least one precordial lead. The clinician must therefore be well versed in recognizing the so-called ECG mimics of acute myocardial infarction, which include left ventricular hypertrophy,left bundle branch block, paced rhythm, early repolarization, pericarditis, hyperkalemia, and ventricular aneurysm.

Cardiac markers

Cardiac markers or cardiac enzymes are proteins that leak out of injured myocardial cells through their damaged cell membranes into the bloodstream. Until the 1980s, the enzymes SGOT and LDH were used to assess cardiac injury. Now, the markers most widely used in detection of MI are *MB* subtype of the enzyme creatine kinase and cardiac troponins T and I as they are more specific for myocardial injury. The cardiac troponins T and I which are released within 4–6 hours of an attack of MI and remain elevated for up to 2 weeks, have nearly complete tissue specificity and are now the preferred markers for asssessing

myocardial damage. Elevated troponins in the setting of chest pain may accurately predict a high likelihood of a myocardial infarction in the near future. New markers such as glycogen phosphorylase isoenzyme BB are under investigation.

The diagnosis of myocardial infarction requires two out of three components (history, ECG, and enzymes). When damage to the heart occurs, levels of cardiac markers rise over time, which is why blood tests for them are taken over a 24-hour period. Because these enzyme levels are not elevated immediately following a heart attack, patients presenting with chest pain are generally treated with the assumption that a myocardial infarction has occurred and then evaluated for a more precise diagnosis.

Angiography

In difficult cases or in situations where intervention to restore blood flow is appropriate, coronary angiography can be performed. A catheter is inserted into an artery (usually the femoral artery) and pushed to the vessels supplying the heart. A radio-opaque dye is administered through the catheter and a sequence of x-rays (fluoroscopy) is performed. Obstructed or narrowed arteries can be identified, and angioplasty applied as a therapeutic measure (see below). Angioplasty requires extensive skill, especially in emergency settings. It is performed by a physician trained in interventional cardiology.

Histopathology

Histopathological examination of the heart may reveal infarction at autopsy. Under the microscope, myocardial infarction presents as a circumscribed area of ischemic, coagulative necrosis (cell death). On gross examination, the infarct is not identifiable within the first 12 hours.

Although earlier changes can be discerned using electron microscopy, one of the earliest changes under a normal microscope are so-called *wavy fibers.* Subsequently, the myocyte cytoplasm becomes more eosinophilic (pink) and the cells lose their transversal striations, with typical changes and eventually loss of the cell nucleus. The interstitium at the margin of the infarcted area is initially infiltrated with neutrophils, then with lymphocytes and macrophages, who phagocytose ("eat") the myocyte debris. The necrotic area is surrounded and progressively invaded by granulation tissue, which will replace the infarct with a fibrous (collagenous) scar (which are typical steps in wound healing). The interstitial space (the space between cells outside of blood vessels) may be infiltrated with red blood cells.

These features can be recognized in cases where the perfusion was not restored; reperfused infarcts can have other hallmarks, such as contraction band necrosis.

Prevention

The risk of a recurrent myocardial infarction decreases with strict blood pressure management and lifestyle changes, chiefly smoking cessation, regular exercise, a sensible diet for patients with heart disease, and limitation of alcohol intake.

Patients are usually commenced on several long-term medications post-MI, with the aim of preventing secondary cardiovascular events such as further myocardial infarctions, congestive heart failure or cerebrovascular accident (CVA). Unless contraindicated, such medications may include:

- Antiplatelet drug therapy such as aspirin and/or clopidogrel should be continued to reduce the risk of plaque rupture and recurrent myocardial infarction.
- Beta blocker therapy such as metoprolol or carvedilol should be commenced. These have been particularly beneficial in high-risk patients such as those with left ventricular dysfunction and/or continuing cardiac ischaemia. β-Blockers decrease mortality and morbidity. They also improve symptoms of cardiac ischemia in NSTEMI.

- ACE inhibitor therapy should be commenced 24–48 hours post-MI in hemodynamically-stable patients, particularly in patients with a history of MI, diabetes mellitus, hypertension, anterior location of infarct (as assessed by ECG), and/or evidence of left ventricular dysfunction. ACE inhibitors reduce
- mortality, the development of heart failure, and decrease ventricular remodelling post-MI.
- Statin therapy has been shown to reduce mortality and morbidity post-MI. The effects of statins may be more than their LDL lowering effects. The general consensus is that statins have plaque stabilization and multiple other ("pleiotropic") effects that may prevent myocardial infarction in addition to their effects on blood lipids.
- The aldosterone antagonist agent eplerenone has been shown to further reduce risk of cardiovascular death post-MI in patients with heart failure and left ventricular dysfunction, when used in conjunction with standard therapies above.
- Omega-3 fatty acids, commonly found in fish, have been shown to reduce mortality post-MI.

Management

A heart attack is a medical emergency which demands both immediate attention and activation of the emergency medical services. The ultimate goal of the management in the acute phase of the disease is to salvage as much myocardium as possible and prevent further complications. As time passes, the risk of damage to

the heart muscle increases; hence the phrase that in myocardial infarction, "time is muscle," and time wasted is muscle lost.

Oxygen, aspirin, glyceryl trinitrate (nitroglycerin) and analgesia . Morphine is classically used if nitroglycerin is not effective due to its ability to dilate blood vessels, which may aids in blood flow to the heart as well as the pain relief it provides. Morphine may also cause hypotension (usually in the setting of hypovolemia), and should be avoided in the case of right ventricular infarction.

Of the front line agents, aspirin and streptokinase have been shown to markedly reduce mortality . Streptokinase activates plasminogen, which is fibrinolytic (see section on thrombolysis below).

Once the diagnosis of myocardial infarction is confirmed, other pharmacologic agents are often given. These include beta blockers, anticoagulation (typically with heparin), and possibly additional antiplatelet agents such as clopidogrel.

First aid

As myocardial infarction is a common medical emergency, the signs are often part of first aid courses. The emergency action principles also apply in the case of myocardial infarction.

When symptoms of myocardial infarction occur, people wait an average of three hours, instead of doing what is recommended: calling for help immediately.

Acting immediately by calling the emergency services can prevent sustained damage to the heart ("time is muscle").

Certain positions allow the patient to rest in a position which minimizes breathing difficulties. A half-sitting position with knees bent is often recommended. Access to more oxygen can be given by opening the window and widening the collar for easier breathing.

Aspirin can be given quickly (if the patient is not allergic to aspirin); but taking aspirin before calling the emergency medical services may be associated with unwanted delay. Aspirin has an antiplatelet effect which inhibits formation of further thrombi (blood clots) that clog arteries. Chewing is the preferred method of administration, so that the Aspirin can be absorbed quickly. Dissolved soluble preparations or sublingual administration can also be used. U.S. guidelines recommend a dose of 162–325 mg. Australian guidelines recommend a dose of

150–300 mg. Glyceryl trinitrate (nitroglycerin) sublingually (under the tongue) can be given if available.

If an automated external defibrillator (AED) is available the rescuer should immediately bring the AED to the patient's side and be prepared to follow its instructions, especially should the victim lose consciousness.

Other general first aid principles include monitoring pulse, breathing, level of consciousness and, if possible, the blood pressure of the patient. In case of cardiac arrest, cardiopulmonary resuscitation (CPR) can be administered.

Automatic external defibrillation (AED)

Since the publication of data showing that the availability of automated external defibrillators (AEDs) in public places may significantly increase chances of survival,many of these have been installed in public buildings, public transport facilities, and in non-ambulance emergency vehicles (e.g. police cars and fire engines). AEDs analyze the heart's rhythm and determine whether the rhythm is amenable to defibrillation("shockable"),as in ventricular tachycardia and ventricular fibrillation.

Reperfusion

Patients who present with suspected acute myocardial infarction and ST segment elevation (STEMI) or new bundle branch block on the 12 lead ECG are presumed to have an occlusive thrombosis in an epicardial coronary artery. They are therefore candidates for immediate reperfusion, either with thrombolytic therapy, percutaneous coronary intervention (PCI) or when these therapies are unsuccessful, bypass surgery.

Individuals without ST segment elevation are presumed to be experiencing either unstable angina (UA) or non-ST segment elevation myocardial infarction (NSTEMI). They receive many of the same initial therapies and are often stabilized with antiplatelet drugs and anticoagulated. If their condition remains (hemodynamically) stable, they can be offered either late coronary angiography with subsequent restoration of blood flow (revascularization), or non-invasive stress testing to determine if there is significant ischemia that would benefit from revascularization. If hemodynamic instability develops in individuals with NSTEMIs, they may undergo urgent coronary angiography and subsequent revascularization. The use of thrombolytic agents is contraindicated in this patient subset, however.

The basis for this distinction in treatment regimens is that ST segment elevations on an ECG are typically due to complete occlusion of a coronary artery. On the other hand, in NSTEMIs there is typically a sudden narrowing of a coronary artery with preserved (but diminished) flow to the distal myocardium. Anticoagulation and antiplatelet agents are given to prevent the narrowed artery from occluding.

At least 10% of patients with STEMI don't develop myocardial necrosis (as evidenced by a rise in cardiac markers) and subsequent Q waves on ECG after reperfusion therapy. Such a successful restoration of flow to the infarct-related

artery during an acute myocardial infarction is known as "aborting" the myocardial infarction. If treated within the hour, about 25% of STEMIs can be aborted.

Thrombolytic therapy

Thrombolytic therapy is indicated for the treatment of STEMI if the drug can be administered within 12 hours of the onset of symptoms, the patient is eligible based on exclusion criteria, and primary PCI is not immediately available. The effectiveness of thrombolytic therapy is highest in the first 2 hours. After 12 hours, the risk associated with thrombolytic therapy outweighs any benefit. Because irreversible injury occurs within 2–4 hours of the infarction, there is a limited window of time available for reperfusion to work.

Thrombolytic drugs are contraindicated for the treatment of unstable angina and NSTEMI and for the treatment of individuals with evidence of cardiogenic shock. Although no perfect thrombolytic agent exists, an ideal thrombolytic drug would lead to rapid reperfusion, have a high sustained patency rate, be specific for recent thrombi, be easily and rapidly administered, create a low risk for intra-cerebral and systemic bleeding, have no antigenicity, adverse hemodynamic effects, or clinically significant drug interactions, and be cost effective. Currently available thrombolyticagentsinclude streptokinase, urokinase, and alteplase (recombinant tissue plasminogen activator, rtPA). More recently, thrombolytic agents similar in structure to rtPA such as reteplase and tenecteplase have been used. These newer agents boast efficacy at least as good as rtPA with significantly easier administration. The thrombolytic agent used in a particular individual is based on institution preference and the age of the patient.

Depending on the thrombolytic agent being used, adjuvant anticoagulation with heparin or low molecular weight heparin may be of benefit. With TPa and related agents (reteplase and tenecteplase), heparin is needed to maintain coronary

artery patency. Because of the anticoagulant effect of fibrinogen depletion with streptokinase and urokinase treatment, it is less necessary there.

Intracranial bleeding (ICB) and subsequent cerebrovascular accident (CVA) is a serious side effect of thrombolytic use. The risk of ICB is dependent on a number of factors, including a previous episode of intracranial bleed, age of the individual, and the thrombolytic regimen that is being used. In general, the risk of ICB due to thrombolytic use for the treatment of an acute myocardial infarction is between 0.5 and 1 percent.

Thrombolytic therapy to abort a myocardial infarction is not always effective. The degree of effectiveness of a thrombolytic agent is dependent on the time since the myocardial infarction began, with the best results occurring if the thrombolytic agent is used within two hours of the onset of symptoms. If the individual presents more than 12 hours after symptoms commenced, the risk of intracranial bleed are considered higher than the benefits of the thrombolytic agent. Failure rates of thrombolytics can be as high as 20% or higher. In cases of failure of the thrombolytic agent to open the infarct-related coronary artery, the patient is then either treated conservatively with anticoagulants and allowed to "complete the infarction" or percutaneous coronary intervention is then performed. Percutaneous coronary intervention in this setting is known as "rescue PCI" or "salvage PCI".

Complications, particularly bleeding, are significantly higher with rescue PCI than with primary PCI due to the action of the thrombolytic agent.

Percutaneous coronary intervention

When performed rapidly by an experienced team, primary PCI restores flow in the culprit artery in more than 95% of patients compared with the spontaneous recanalization rate of about 65%. The use of percutaneous coronary intervention as a therapy to abort a myocardial infarction is known as primary PCI. The goal of primary PCI is to open the artery as soon as possible, and preferably within 90 minutes of the patient presenting to the emergency room. This time is referred to as the door-to-balloon time.

Primary PCI involves performing a coronary angiogram to determine the anatomical location of the infarcting vessel, followed by balloon angioplasty (and

frequently deployment of an intracoronary stent) of the thrombosed arterial segment. In some settings, an extraction catheter may be used to attempt to aspirate the thrombus prior to balloon angioplasty. While the use of intracoronary stents do not improve the short term outcomes in primary PCI, the use of stents is widespread because of the decreased rates of procedures to treat restenosis compared to balloon angioplasty .

Adjuvant therapy during primary PCI include intravenous heparin, aspirin, and clopidogrel. The use of glycoprotein IIb/IIIa inhibitors are often used in the setting of primary PCI to reduce the risk of ischemic complications during the procedure. Due to the number of antiplatelet agents and anticoagulants used during primary PCI, the risk of bleeding associated with the procedure are higher than during an elective PCI.

Coronary artery bypass surgery

Despite the guidelines, emergency bypass surgery for the treatment of an acute myocardial infarction (MI) is less common than PCI or medical management.

Emergency coronary artery bypass graft surgery (CABG) is usually undertaken to simultaneously treat a mechanical complication, such as a ruptured papillary muscle, or a ventricular septal defect, with ensueing cardiogenic shock. In uncomplicated MI, the mortality rate can be high when the surgery is performed immediately following the infarction. If this option is entertained, the patient should be stabilized prior to surgery, with supportive interventions such as the use of an intra-aortic balloon pump. In patients developing cardiogenic shock after a myocardial infarction, both PCI and CABG are satisfactory treatment options, with similar survival rates.

Coronary artery bypass surgery involves an artery or vein from the patient being implanted to bypass narrowings or occlusions on the coronary arteries. Several arteries and veins can be used, however internal mammary artery grafts have demonstrated significantly better long-term patency rates than great saphenous vein grafts. In patients with two or more coronary arteries affected, bypass surgery is associated with higher long-term survival rates compared to percutaneous

interventions. In patients with single vessel disease, surgery is comparably safe and effective, and may be a treatment option in selected cases. Bypass surgery has higher costs initially, but becomes cost-effective in the long term. A surgical bypass graft is more invasive initially but bears less risk of recurrent procedures (but these may be again minimally invasive).

Monitoring for arrhythmias

Additional objectives are to prevent life-threatening arrhythmias or conduction disturbances. This requires monitoring in a coronary care unit and protocolised administration of antiarrhythmic agents. Antiarrhythmic agents are typically only given to individuals with life-threatening arrhythmias after a myocardial infarction and not to suppress the ventricular ectopy that is often seen after a myocardial infarction.

Rehabilitation

Cardiac rehabilitation aims to optimize function and quality of life in those afflicted with a heart disease. This can be with the help of a physician, or in the form of a cardiac rehabilitation program.

Physical exercise is an important part of rehabilitation after a myocardial infarction, with beneficial effects on cholesterol levels, blood pressure, weight, stress and mood. Some patients become afraid of exercising because it

might trigger another infarct. Patients are stimulated to exercise, and should only avoid certain exerting activities Local authorities may place limitations on driving motorised vehicles Some people are afraid to have sex after a heart attack. Most people can resume sexual activities after 3 to 4 weeks. The amount of activity needs to be dosed to the patient's possibilities.

New therapies under investigation

Patients who receive stem cell treatment by coronary artery injections of stem cells derived from their own bone marrow after a myocardial infarction (MI) show improvements in left ventricular ejection fraction and end-diastolic volume not seen with placebo. The larger the initial infarct size, the greater the effect of the infusion. Clinical trials of progenitor cell infusion as a treatment approach to ST elevation MI are proceeding.

There are currently 3 biomaterial and tissue engineering approaches for the treatment of MI, but these are in an even earlier stage of medical research, so many questions and issues need to be addressed before they can be applied to patients. The first involves polymeric left ventricular restraints in the prevention of heart failure. The second utilizes *in vitro* engineered cardiac tissue, which is subsequently implanted *in vivo*. The final approach entails injecting cells and/or a scaffold into the myocardium to create *in situ* engineered cardiac tissue.

Complications

Complications may occur immediately following the heart attack (in the acute phase), or may need time to develop (a chronic problem). After an infarction, an obvious complication is a second infarction, which may occur in the domain of another atherosclerotic coronary artery, or in the same zone if there are any live cells left in the infarct.

Congestive heart failure

A myocardial infarction may compromise the function of the heart as a pump for the circulation, a state called heart failure. There are different types of heart failure; left- or right-sided (or bilateral) heart failure may occur depending on the affected part of the heart, and it is a low-output type of failure. If one of the heart valves is affected, this may cause dysfunction, such as mitral regurgitation in the case of left-sided coronary occlusion that disrupts the blood supply of the papillary muscles. The incidence of heart failure is particularly high in patients with diabetes and requires special management strategies.

Myocardial rupture

Myocardial rupture is most common three to five days after myocardial infarction, commonly of small degree, but may occur one day to three weeks later. In the modern era of early revascularization and intensive pharmacotherapy as treatment

for MI, the incidence of myocardial rupture is about 1% of all MIs . This may occur in the free walls of the ventricles, the septum between them, the papillary muscles, or less commonly the atria. Rupture occurs because of increased pressure against the weakened walls of the heart chambers due to heart muscle that cannot pump blood out effectively. The weakness may also lead to ventricular aneurysm, a localized dilation or ballooning of the heart chamber.

Rupture is usually a catastrophic event that may result a life-threatening process known as cardiac tamponade, in which blood accumulates within the pericardium or heart sac, and compresses the heart to the point where it cannot pump effectively. Rupture of the intraventricular septum (the muscle separating the left and right ventricles) causes a ventricular septal defect with shunting of blood through the defect from the left side of the heart to the right side of the heart, which can lead to right ventricular failure as well as pulmonary overcirculation. Rupture of the papillary muscle may also lead to acute mitral regurgitation and subsequent pulmonary edema and possibly even cardiogenic shock.

Life-threatening arrhythmia

Since the electrical characteristics of the infarcted tissue change arrhythmias are a frequent complication . The re-entry phenomenon may cause rapid heart rates (ventricular tachycardia and even ventricular fibrillation), and ischemia in the electrical conduction system of the heart may cause a complete heart block (when the impulse from the sinoatrial node, the normal cardiac pacemaker, does not reach the heart chambers).

Pericarditis

As a reaction to the damage of the heart muscle, inflammatory cells are attracted. The inflammation may reach out and affect the heart sac. This is called pericarditis. In Dressler's syndrome, this occurs several weeks after the initial event.

Cardiogenic shock

A complication that may occur in the acute setting soon after a myocardial infarction or in the weeks following it is cardiogenic shock. Cardiogenic shock is defined as a hemodynamic state in which the heart cannot produce enough of a cardiac output to supply an adequate amount of oxygenated blood to the tissues of the body.

While the data on performing interventions on individuals with cardiogenic shock is sparse, trial data suggests a long-term mortality benefit in undergoing revascularization if the individual is less than 75 years old and if the onset of the acute myocardial infarction is less than 36 hours and the onset of cardiogenic shock is less than 18 hours. If the patient with cardiogenic shock is not going to be revascularized, aggressive hemodynamic support is warranted, with insertion of an intra-aortic balloon pump if not contraindicated. If diagnostic coronary angiography does not reveal a culprit blockage that is the cause of the cardiogenic shock, the prognosis is poor .

Prognosis

The prognosis for patients with myocardial infarction varies greatly, depending on the patient, the condition itself and the given treatment. Using simple variables which are immediately available in the emergency room, patients with a higher risk of adverse outcome can be identified. For example, one study found that 0.4% of patients with a low risk profile had died after 90 days, whereas the mortality rate in high risk patients was 21.1% .

Although studies differ in the identified variables, some of the more reproduced risk stratifiers include age, hemodynamic parameters (such as heart failure, cardiac arrest on

admission, systolic blood pressure, or Killip class of two or greater), ST-segment deviation, diabetes, serum creatinine concentration, peripheral vascular disease and elevation of cardiac markers. Assessment of left ventricular ejection fraction may increase the predictive power of some risk stratification models. The prognostic importance of Q-waves is debated. Prognosis is significantly worsened if a mechanical complication (papillary muscle rupture, myocardial free wall rupture, and so on) were to occur.

RELATED STUDIES

1. Reduction in QT interval dispersion by successful thrombolytic therapy in acute myocardial infarction. TEAM-2 Study Investigators FL Moreno, T Villanueva, LA Karagounis and JL Anderson. Circulation,1994; Vol 90, 94-100

BACKGROUND: QT dispersion (QTd, equals maximal minus minimal QT interval) on a standard ECG has been shown to reflect regional variations in ventricular repolarization and is significantly greater in patients with than in those without arrhythmic events. METHODS AND RESULTS: To assess the effect of thrombolytic therapy on QTd, we studied 244 patients (196 men; mean age, 57 +/- 10 years) with acute myocardial infarction (AMI) who were treated with streptokinase (n = 115) or anistreplase (n = 129) at an average of 2.6 hours after

symptom onset. Angiograms at 2.4 +/- 1 hours after thrombolytic therapy showed reperfusion (TIMI grade > or = 2) in 75% of patients. QT was measured in 10 +/- 2 leads at 9 +/- 5 days after AMI by using a computerized analysis program interfaced with a digitizer. QTd, QRSd, JT (QT minus QRS), and JT dispersion (JTd, equals maximal minus minimal JT interval) were calculated with a computer. There were significant differences in QTd (96 +/- 31, 88 +/- 25, 60 +/- 22, and 52 +/- 19 milliseconds; P < or = .0001) and in JTd (97 +/- 32, 88 +/- 31, 63 +/- 23, and 58 +/- 21 milliseconds; P = .0001) but not in QRSd (25 +/- 10, 22 +/- 7, 28 +/- 9,

and 24 +/- 9 milliseconds; P = .24) among perfusion grades 0, 1, 2, and 3, respectively. Similar results were obtained comparing TIMI grades 0/1 with 2/3 and 0/1/2 with 3. Patients with left anterior descending (versus right and left circumflex) coronary artery occlusion showed significantly greater QTd (70 +/- 29 versus 59 +/- 27 milliseconds, P = .003) and JTd (74 +/- 30 versus 63 +/- 27 milliseconds, P = .004). Similarly, patients with anterior (versus inferior/lateral) AMI showed significantly greater QTd (69 +/- 30 versus 59 +/- 27 milliseconds, P = .006) and JTd (73 +/- 30 versus 63 +/- 27 milliseconds, P = .007). Results did not change when Bazett's QTc or JTc was substituted for QT or JT or when ANOVA included adjustments for age, sex, drug assignment, infarct site, infarct vessel, and number of measurable leads. On ANCOVA, the relation of QTd or JTd and perfusion grade was not influenced by heart rate. CONCLUSIONS: Successful

thrombolysis is associated with less QTd and JTd in post-AMI patients. The results are equally significant when either QT or JT is used for analysis. These data support the hypothesis that QTd after AMI depends on reperfusion status as well as infarct site and size. Reduction in QTd and its corresponding risk of ventricular arrhythmia may be mechanisms of benefit of thrombolytic therapy.

2. Charles Antzelevitch et al- Cardiac repolarization. The long and short of it* *Europace20057(s2):S3-S9;

Heterogeneity of transmural ventricular repolarization in the heart has been linked to a variety of arrhythmic manifestations. Electrical heterogeneity in ventricular myocardium is due to ionic distinctions among the three principal cell types: Endocardial, M and Epicardial cells. A reduction in net repolarizing current generally leads to a preferential prolongation of the M cell action potential. An increase in net repolarizing current can lead to a preferential abbreviation of the action potential of right ventricular epicardium or left ventricular endocardium.These changes can result in amplification of transmural heterogeneities of repolarization and thus predispose to the development of potentially lethal reentrant arrhythmias

3.Assessment of QT Dispersion for Prediction of Mortality or Arrhythmic Events After Myocardial Infarction Markus Zabel, MD; Thomas Klingenheben, MD; Michael R. Franz, MD, PhD; ; Stefan H. Hohnloser, MD

Circulation. 1998;97:2543-2550.) © 1998 American Heart Association, Inc.

In 280 consecutive infarct survivors, the 12-lead ECG was optically scanned and digitized for analysis of QTD (QT_{max}-QT_{min}) and 25 other repolarization

variables, including recently developed and validated parameters such as the T peak–to–T end interval and the area under the T wave. In addition, a variety of established risk stratifiers were assessed. After a mean follow-up period of 32±10 months, 30 patients reached one of the prospectively defined study end points (death, ventricular tachycardia, or resuscitated ventricular fibrillation). Comparisons between event and nonevent patients by means of Kaplan-Meier event probability analyses revealed that none of the ECG dispersion variables were of discriminative value. In contrast, variables such as left ventricular ejection fraction (P=0.007), mean 24-hour heart rate (P=0.022), or heart rate variability (P=0.007) proved to be potentially useful risk stratifiers in this patient population. On multivariate analysis, only LVEF, heart rate variability, and a history of thrombolysis were independent predictors of outcome.

4.Short-and Long-Term Reproducibility of QT, QTc, and QT Dispersion Measurement in Healthy Subjects **JOSEF KAUTZNER , GANG YI , A. JOHN, CAMM, MAREK MALIK** **Pacing and Clinical Electrophysiology**

Volume 17 Issue 5**, Pages 928 - 937** © 2009 Wiley Periodicals, Inc.

The study investigated interobserver and intrasubject reproducibility of QT interval duration and dispersion measured in standard 12-lead ECGs recorded at 25 mm/sec. Twenty-eight healthy volunteers were studied. Each undenvent four ECG

recordings, which were performed 1, 7, and 30 days apart. Two independent observers analyzed each ECG record. In each lead with a distinguishable T wave pattern, the RR interval, Q-peak of T interval, and Q-end of T interval were measured using a digitizing board with a 0.1-mm resolution. From each recording the following measures were derived: the maximum, minimum, and mean QT interval; maximum, minimum, and mean heart rate corrected QT interval (QTc); QT and QTc dispersion (the difference between the maximum and minimum QT interval among the 12 leads); and adjusted QT and QTc dispersion (dispersion divided by the square root of the number of leads measured). The interobserver and short-term (1 day) and long-term (1 week and 1 month) reproducibility of individual indices was assessed by computing the relative errors and comparing them by a standard sign test. In addition, the distributions of maximum and

minimum QTc values among electrocardiographicleads, and the differences between QT-end and QT-peak based measurements were investigated. The results showed that: (1) the measurement of the QT interval from standard ECG recordings is feasible and not operator dependent (interobserver relative error <4%); (2) the duration of the QT interval in healthy volunteers is stable and its short- and long-term reproducibility is high (intrasubject relative error < 6%); (3) parameters that characterize dispersion of the QT interval in the 12-lead ECG are highly nonreproducible, both between subsequent recording (relative error of

25%–35%) and between observers (relative error 28%–33%), the reproducibility of QT dispersion is significantly lower than that of QT duration ($P < 0.01$); and (4) the duration of the entire QT interval correlates only weakly with the duration of the Q-peak of T interval.

5.QT Dispersion and Early Arrhythmic Risk During Acute Myocardial Infarction Paventis et al, Angiology, Vol. 50, No. 3, 209-215 (1999)

Three hundred three patients with acute myocardial infarction and a control group of 297 healthy subjects were studied. QT and QTc dispersion were determined on the electrocardiogram taken after 12 hours and on days 3 and 10 after symptoms onset and on the electrocardiogram taken in the control group. The average values of QT and QTc dispersions (ms) were as follows: 70.5 ±42.5-87 ±45.6 (12th hour),

66.7 ±37.6-76.8±43.6 (day 3), 68.8 ±42.7-76.8 ±42.8 (day 10), versus 43 ±13.2-53.9 ±16.2 (control group). There were statistically significant differences between QT and QTc dispersion recorded in normal subjects and in each of the three electrocardiograms taken in patients with infarction. A greater QT dispersion was recorded in patients with anterior infarction (78.9 ±38.5 vs 64.9 ±42.8 in inferior/lateral infarction). In the first 3 days QT dispersion was not different in patients treated and untreated with throm bolysis, whereas on day 10 it was greater in untreated patients (74.9 ±45.3 vs 60.5 ±37.2). Creatine kinase peak level did not influence QT dispersion. In the first 72 hours of infarction, 37 patients developed ventricular fibrillation or sustained ventricular tachy cardia. Higher early values of QT and QTc dispersion were found in patients who developed severe ventricular arrhythmias (107.8 ±62 and 124.8 ±67.5 ms) than in patients without serious arrhythmias (62.9 ±32.2 and 80.1 ±37.9 ms).

6.QT dispersion as a risk factor for sudden cardiac death and fatal myocardial infarction in a coronary risk population.M. Mänttäri, L. Oikarinen, V. Manninen, M. Viitasalo *Heart* 1997;**78**:268-272

At study baseline, QT dispersion was similar in all victims and controls. When estimated from the pre-event ECG on average 14 months before death, the risk of sudden cardiac death in the highest QTPEAK (up to the peak of the T wave)

dispersion tertile (> or = 50 ms) was 6.2-fold (95% confidence interval 1.7 to 23.5) comparedwith the risk in the lowest tertile (< or = 30 ms), and 4.9-fold (1.2 to 19.5) after adjustment for the presence of left ventricular hypertrophy, while QTPEAK dispersion could not predict fatalmyocardial infarction. QTEND dispersion (up to the end of the T wave) in pre-event ECGs could not discriminate victims of either sudden cardiac death or fatal myocardial infarction from their matched controls. CONCLUSIONS: In middle aged men with a normal conventional QT interval in 12-lead resting ECG, increased QTPEAK dispersion is an independent risk factor for sudden cardiac death, but not for fatal myocardial infarction.

7.QT-interval dispersion in acute myocardial infarction is only shortened by thrombolysis in myocardial infarction grade 2/3 reperfusion

Nikiforos, Hatzisavvas, Pavlides, Voudris, Vassilis P. Vassilikos, Manginas, Hatzeioakim, Stefanos Foussas, Iliodromitis, Hatseras, Kremastinos, Cokkinos,

Background: Increased QT interval dispersion (QTd) has been found in patients with acute myocardial infarction (AMI). In previous studies this has been shown to decrease with thrombolysis.

Hypothesis: The aim of this study was to compare the effects of reperfusion by primary percutaneous transluminal coronary angioplasty (PTCA) and by thrombolysis on QTd and correlate these results with the degree of reperfusion.

Methods: We studied 60 patients with a first AMI. The study cohort included 40 consecutive patients who had received thrombolysis (streptokinase or rt-PA); 20 additional consecutive patients with successful primary PTCA, all with preselected Thrombolysis in Myocardial Infarction (TIMI) grade 3 flow by predefined selection criteria (12 stents); and 20 controls. A 12-lead ECG for QTd calculation was recorded before thrombolysis or PTCA and immediately after the procedure.

All values were corrected according to Bazett's formula (QTcd). QTd and QTcd values before and after each procedure in three groups and the respective percent changes of QTd and QTcd were compared separately.

Results: QTd and QTcd were significantly increased before thrombolysis/PTCA versus normals. An angiogram performed after thrombolysis showed adequate reperfusion (TIMI grade 2/3) in 20 patients, while in the other 20 only TIMI 0/1 reperfusion was achieved. Thrombolysis-TIMI flow 2/3 and PTCA significantly reduced QTd (from 68 ± 10 to 35 ± 8 ms, $p < 0.001$, QTd = 48 ± 11%, in the Thr-TIMI flow 2/3 group, and from 79 ± 11 to 38 ± 9 ms, $p < 0.001$, QTd = 52 ± 9%, in

the PTCA group), while in the Thr-TIMI flow 0/1 group no significant changes were recorded. A percent QTd decrease > 30 s had 96% sensitivity, 85% specificity, and 93% positive and 94% negative predictive value, respectively, for TIMI 2/3 flow

8.**QT dispersion and early arrhythmic risk during acute myocardial** infarction.Ciolli A, Di Lorenzo M, Bevilacqua U, Lo Sardo G, Tripi M, Fidati R, Palamara A**.** G Ital Cardiol. 1999 Dec;29(12):1438-44.

We studied 101 patients with acute myocardial infarction and a control group of 97 healthy subjects. . The average values of QT and QTc dispersion (measured hereafter in milliseconds, ms) were as follows: 70.5 +/- 42.5-87 +/- 46.6 (after 12 hours), 66.5 +/- 37.8-76.9 +/- 43.5 (on day 3), 68.9 +/- 42-76.3 +/- 43.8 (on day 10) and 44 +/- 13.4-54.2 +/- 16.3 (in control group). We observed statistically significant differences in QT and QTc dispersion between the electrocardiogram of normal subjects and each of the three electrocardiograms performed on patients with infarction ($p < 0.0005$, $p < 0.005$). . Creatine kinase peak level, sex and age of the patients did not influence QT dispersion. Thirteen patients (12.8%) developed severe ventricular arrhythmias within 72 hours after infarction: 8 patients (7.9%) had ventricular fibrillation and 5 patients (4.9%) had sustained ventricular tachycardia. We found higher early QT and QTc dispersion values in patients who developed severe ventricular arrhythmias (108.8 +/- 63.2 and 125.8 +/- 68.5) with respect to patients who did not (63.3 +/- 32.9 and 80.8 +/- 38.9, $p < 0.0005$, $p < 0.0005$).

AIMS OF THE STUDY

1.To calculate the QT, QTc, QTd, QTcd in all patients with acute myocardial infarction

2. To determine the difference of QT parameters in patients treated with thrombolytic agents(streptokinase) against those not treated with thrombolytic agents(streptokinase)

MATERIALS AND METHODS

102 patients admitted in KAPV Government Medical College Hospital, Tiruchirapalli for Acute Myocardial infarction were taken up for the study. All patients were followed for a period of 8±2 days during their stay in the hospital. The study group was chosen taking into consideration of the following criteria

INCLUSION CRITERIA :

1. Acute Myocardial infarction

* Chest pain >30 minutes

* Chest pain not relieved by rest or nitrates

* ST elevation >1mm or 0.1mv in ≥2 limb leads

  ST elevation >2mm or 0.2mv in ≥ 2 precordial leads

* NSTEMI

2. Treatment with Thrombolytic therapy (streptokinase) / without Thrombolytic therapy

EXCLUSION CRITERIA :

1. The contraindications for thrombolytic therapy for those patients who were treated with thrombolytic therapy

2. Drugs affecting QT interval eg.Quinidine,procainamide,tricyclics&tetracyclics depressants,astemizole,digitalis

3. Hypertrophic cardiomyopathy, Acute carditis

4. Atrial fibrillation, Bundle branch blocks

5 . Prior coronary bypass surgery

6. Serum potassium <3.5 mmol/l or > 5.0mmol/l

7. Congenital long QT Syndromes

Jervell-Lange-Neilson Syndrome(deafness,syncope &sudden death with long QT interval)

Romano-Ward Syndrome(similar to the above Syndrome but without deafness)

METHODS In Patients admitted for Acute Myocardial infarction, a standard 12 lead ECG was taken at paper speed of 25 mm/s at admission and before discharge(day 8±2).From these ECG's taken in all 102 patients the following parameter were calculated.

1.QT INTERVAL: It was measured from the first deflection of the QRS complex to the point of T wave offset,defined by the return of terminal T wave to the isoelectric TP baseline. It represents the total duration of ventricular activity i.e the sum of ventricular depolarisation and repolarisation

2. QTc INTERVAL:QT interval shortens with tachycardia and lengthens with bradycardia. So it is corrected using **Bazett's formula**.RR interval is measured between two consecutive R waves. **QTc** = $\frac{QT}{\sqrt{RR}}$. Normal range of QTc is 0.35 to 0.43 sec

3.QT & QTc Dispersions: They are defined as the difference between the maximum and minimum QT,QTc in each of the 12 leads studied.The QT parameters were correlated taking into the following variables- site of infarction, age of the patient, diabetes, HT, smoking, alcoholism. Since the peak creatine kinase level have no correlation with QT parameters ,it was not considered.

TABLES AND CHART

TABLE: 1 COMPOSITION OF THE STUDY POPULATION

SITE OF INFARCTION	TOTAL	SEX		TYPE OF INFARCTION	
		MALE	FEMALE	STEMI	NSTEMI
1) Anterior wall	50	46	4	44	6
2) Extensive anterior	10	10	0	10	0
3) Inferior :	42	36	6	42	0
i) with RVMI	24	20	4	24	0
ii) With posterior wall	4	4	0	4	0

iii)Infero lateral	4	4	0	4	0
TOTAL	**102**	**92**	**10**	**96**	**6**

TABLE: 2 RISK FACTORS AND MYOCARDIAL INFARCTION

SITE OF INFARCT	DIABETES MELLITUS	HYPERTENSION	SMOKING	ALCOHOLISM
1)Anterior	16	15	23	21
2) Extensive anterior	4	3	3	2
3)Iinferior	13	12	11	5
TOTAL	**33**	**30**	**37**	**28**

TABLE: 3 QT PARAMETERS AND THROMBOLYSIS

TREATMENT	AT ADMISSION		D8 ± 2	
	QTd	**QTed**	**QTed**	**QTed**
Thrombolysed	80.71	93.68	39.28	46.5
NotThrombolysed	72.17	77.95	68.69	73.78

P Values	QTd	QTcd
Anterior wall	0.0009756	0.002549
Inferior wall	0.0002256	0.0002391

QT PARAMETERS IN THROMBOLYSED PATENTS

AND SITE OF INFARCTION

	AT ADMISSION		**D8 ± 2**	
SITE				
	QTd	**QTed**	**QTed**	**QTed**
1)Anterior	83.33	99.16	43.3	50.83
2) Extensive anterior	84	107	40	51.4
3) Inferior	76.36	81.63	34.54	39.54
Total	**80.71**	**93.68**	**39.28**	**46.5**

QT PARAMETERS AND SITE OF INFARCTION IN NOT

THROMBOLYSED PATENTS

	AT ADMISSION		**D8 ± 2**	
SITE				
	QTd	**QTcd**	**QTd**	**QTcd**
Anterior wall	74.28	80.71	68.57	74.42
Inferior wall	68.8	73.44	68.88	72.77

Total	**72.17**	**77.95**	**68.69**	**73.78**

TABLE :4 AGE AND SITE OF INFARCTION

Age	Anterior	Extensive Anterior	Inferior	Total
20-29	**2**	**2**	**6**	**10**
30-39	**6**	**-**	**6**	**12**
40-49	**18**	**6**	**8**	**32**
50-59	**10**	**2**	**16**	**28**
60-69	**10**	**-**	**6**	**16**
70-79	**4**	**-**	**-**	**4**
Total	**50**	**10**	**42**	**102**

Pvalues	QTd	QTcd

40-49	**0.0103**	**0.03123**
50-59	**0.02157**	**0.053**
60-69	**0.0351**	**0.03261**

TABLE 5:AGE & QT PARAMETERS IN THROMBOLYSED PATIENTS

AGE	AT ADMISSION		D8±2	
	QTd	QTcd	QTd	QTcd
20-29	80	91.75	40	46.75
30-39	80	87	20	24
40-49	82.22	98	42.22	47.88
50-59	71.42	84.57	37.14	45.85
60-69	83.66	100.33	46.66	53.33
70-79	90	87	40	46

IN NOT THROMBOLYSED PATIENTS

AGE	AT ADMISSION		D8±2	
	QTd	QTcd	QTd	QTcd
20-29	80	78	80	92
30-39	72	78.8	72.	78
40-49	71.42	80.85	68.57	73.42
50-59	65.71	69.85	62.85	66.85
60-69	100	99	80	89.5
70-79	60	66	60	64

RESULTS AND OBSERVATION

1.Composition of the Study Population

A total of 102 patients were taken up for the study.Of these 56 patients were treated with thrombolytic therapy and 46 patients were not treated with thrombolytic therapy.There were 92 males (90%) and 10 females(10%),Anterior wall infarction constituted 49%,extensive anterior 10% and inferior wall 41%.There were only 6 patients with NSTEMI.

2.Age and QT parameters

The QT parameters were correlated among different age groups. The QT parameters showed significant variation between the patients treated with thrombolytic therapy and not treated with thrombolytic therapy, in age groups 40-49,50-59,60-69.The other age groups did not show significant statistical variation,as the number of patients was small.

3.QT parameters and Thrombolysis and Site of Infarction.

The QT parameters were correlated among study groups and it was found that there was significantly greater reductions in QT parameters at day 8±2 in patients treated with thrombolytic therapy when compared with not treated with thrombolytic therapy.It was noted that anterior wall infarction show significantly greater QT,QTc dispersions when compared with inferior wall infarction.These differences int he QT parameters were all statistically significant.

DISCUSSION

It has been suggested that QT dispersion (maximal minus minimal QT interval calculated on a standard 12-lead electrocardiogram) could reflect regional variations of ventricular repolarization and could provide a substrate for reentry ventricular arrhythmias. Previous studies have proven that successful thrombolysis significantly decreases the QT parameters and thereby the arrythmogenic potential and hence it decreases the risk of sudden cardiac death in patients with acute myocardial infarction.

The present study evaluates QT dispersion in patients with acute myocardial infarction treated with thrombolytic therapy when compared with those who were not treated with thrombolytic therapy. As given in most of the studies cited in the review of literature male patients out numbered the females,constituting 90 % of the study population . Sex and age of the patients did not influence QT dispersion

In the first 3 days QT dispersion was not different in patients treated and untreated with thrombolysis, whereas on day 8±2 it was greater in untreated patients .When correlated totally with all walls taken together or individually, there were significantly greater reduction in QT,QTc dispersions in patients treated with thrombolytic therapy when compared with those who were not treated with thrombolytic therapy. This correlates well with all studies depicted (consistent with yonus et al ,1996,Paventi.S et al 1994)

The anterior acute myocardial infarction showed significantly greater QT parameters when compared with inferior acute myocardial infarction patients .And there was significantly greater reductions in QT parametersin patients treated with thrombolytic therapy when compared with those who were not treated with thrombolytic therapy at day 8±2 (consistent with I.Lorincz,C.Kun,Z.Karanyi,F.Norum).These reductions were also statistically significant.

CONCLUSION

1. There were significantly greater mean QT,QTc dispersions in the early hours of Acute Myocardial infarction

2. Patients with anterior acute myocardial infarction showed significantly greater QT parameters when compared with inferior acute myocardial infarction patients

3. There were significantly greater reduction in QT,QTc dispersions after treatment with streptokinase than without it.

4. QT,QTc dispersions are greatest in the early hours of acute myocardial infarction and fall with time and successful thrombolysis

5.These results can be taken into accont in the risk stratificatiojn for malingnant ventricular tachyarrythymias and they are another evidence for the benefit of thrombolytic therapy in patients with acute myocardial infarction

PROFORMA

Name Age Sex

Address Occupation

DOA:- Ward IP.No

History Duration

Chest pain

Palpitation

Dyspnoea

Syncope

Cough / Expectoration

Past History Drug intake :

Known IHD HT

HT IHD

DM DM

Dyslipidemia Others

Personal History

Smoker

Alcoholic

Addiction

Others

Family History

IHD

Sudden Cardiac Death

Clinical Examination

Evidence of Peripheral vascular Disease

Evidence of Hyperlipdemia

Obesity

Pedal odema

Deafness

PR:

BP:

JVP:

Cardiovascular System

S1, S2

Gallop

Murmur

Respiratory System

Breath Sounds

Basal Creps

Initial ECG

Type of information: Q Wave

Non Q Wave

Wall Involvement

Inferior wall

Anterior wall

Anteroseptal

Antero lateral

Posterior

Others

Etopics Yes / No

Median Delay :

Thrombolysis Yes / No

Investigations:

Blood Sugar

- Fasting
- Post Prandial

Blood urea

Sr. Creatinine

Sr. Electrolytes Na^+ K^+ $HC0_3$

Sr. Cholesterol

Sr. Calcium

Sr. Phosphorous

CPK

CPK. MB

QT Studies in 12 Hours ECG

Q – Wave

QT Segment Changes	QT
T Wave Changes	QTc
Arrhythmias Recorded in monitor	QTd
Blocks	QTcd

Bradycardia

AV Dissociation

Ventricular Arrhythmias

Ventricular Tachycardia	Yes / No
Ventricular Fibrillation	Yes / No

Sudden Death

Yes / No

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