Introduction

Asymptomatic mild increase in creatinine kinase (CK) and its isoenzyme creatinine kinase of myocardial band (CK-MB) that occurs after elective percutaneous transluminal coronary angioplasty (PTCA) that have been regarded as a common and without prognostic consequences for patients. However, studies demonstrated that patients with only minor elevations in CK-MB had a worse long-term outcome than patients without CK-MB increase *(Ravklide et al., 1994).*

Asymptomatic increase of cardiac enzymes levels in patients with chronic stable angina undergoing PTCA with or without stenting has gained wider interest. A few studies, which addressed this problem, showed that Periprocedural increase in cardiac markers levels was associated with an unfavorable clinical outcome *(Polanzyk et al., 1998).*

The incidence of increase in cardiac troponins following elective percutaneous coronary intervention (PCI) varies between 20% and 60%. Cardiac troponin I and T, which are parts of contractile apparatus of myocardial

muscle, have been used as sensitive markers to detect myocardial injury *(Shyu et al., 1998)*.

Cardiac troponin I is more sensitive and specific than CK-MB for diagnosing minor myocardial injury. The results of studies examining the prognostic role of Periprocedural cardiac troponins elevation are inconclusive. Some studies demonstrate that even a small increase of cardiac troponin I and T after PCI were sensitive markers of adverse cardiac events *(Saadeddin and Habbab, 2001)*.

Aim of the Work

Study of the cardiac troponin I and T elevation after elective successful PTCA with or without stenting as a detector of minor myocardial injury.

Serum Markers of Myocardial Necrosis

The Ideal Marker:

To be useful for diagnosis in the clinical setting, a serum marker of myocardial necrosis should be rapidly released early after the onset of ischemic symptoms and remain elevated for 12 to 24 hours in the serum, but not so long as to preclude detection of recurrent myocardial injury after an index event.

It should be released in proportion to the degree of myocardial injury and should be very specific for myocardial cell damage versus skeletal muscle or other tissue damage (that is, found in cardiac muscle but not in other tissues).

To have a very sensitive, rapid, quantitative assay for the marker would be ideal, but semi quantitative or qualitative whole-blood bedside assays are particularly useful in emergency departments, where online decisions can facilitate rapid identification and triage of ACS patients.

Finally, for use in short and long-term risk stratification, there should be a correlation between outcome and the presence or absence of a marker in the serum or the degree of elevation of the marker above the normal value *(Callif & Ohman 1992)*.

Myoglobin:

Myoglobin is a 17.8-kDa heme protein that is found in all striated muscle, including cardiac tissue. It is released early after the onset of ischemia, is usually elevated at between 1 and 2 hours, peaks at 6 to 12 hours, and returns to baseline by 12 to 24 hours because of rapid renal clearance.

A pattern of discontinuous release of myoglobin consisting of multiple peaks or the staccato phenomenon occurs in patients who have suffered A.M.I. *(Drexel et al., 1983)*. This pattern of myoglobin elaboration may reflect cyclical spontaneous coronary reocclusion and reperfusion of the ischemic myocardium leading to bursts of myoglobin release. Thus, early treatment with thrombolytic therapy has been shown to decrease the number of staccato peaks *(Gasser et al., 1987)*.

Because it is found in all striated muscle, it is not specific for cardiac injury and may be "falsely" elevated in skeletal muscle trauma or skeletal myopathies. Further, because it is excreted renally, it may be falsely positive in patients with renal failure. However, the diagnostic sensitivity and predictive value of a negative result are high in the first hours after MI *(Roxin et al., 1984)*.

Although sensitive, rapid commercial assays are available, as a marker for cardiac muscle necrosis, it suffers from its lack of specificity and rapid renal clearance. Therefore, even though it may be positive very early after injury, and it can not provide a sole basis for a decision of diagnosis *(Ohman et al, 1982)*.

Myosin fragments:

Myosin consists of six proteins: two heavy chains (M.W. 200 kDa each) and two pairs of dissimilar proteins (M.W. 20 kDa to 26 kDa each) designated myosin light chain I and II (MLC-I and MLC-II). Both participate in the regulation of the interaction of actin and myosin predominantly by modulating changes in calcium flux *(Weeds and Pope, 1971)*.

Myosin light chains (MLCs):

At least two forms of MLCs exist in the ventricles and atria, and at least three forms of MLCs are found in skeletal muscle, MLC fragments are sensitive markers of myocardial injury, because prolonged elevation permit retrospective detection for up to 2 weeks *(Katus et al., 1984)*.

The contention that measurement of MLC is more sensitive for the detection of AMI than either total CK or CK-MB probably is due to this prolonged diagnostic

window rather than a greater amount of protein release per gram of injured tissue *(Katus et al., 1988)*.

Myosin heavy chains (MHCs):

Myosin heavy chains are larger fragments that dissociate from other structural proteins before release. Levels of MHC are not present in plasma until 2 days after the event, peak levels occur 5 to 6 days later. Elevation persists for up to 10 days allowing for a prolonged retrospective determination of myocardial necrosis *(Leger et al., 1990)*.

Creatine kinase:

Creatine kinase (CK) is a dimmer composed of two subunits, each with a molecular weight of about 40 KDa. (~85 KDa. molecular weight) is a ubiquitous enzyme in the cytosol of striated muscle (and many other tissues) that catalyzes the reversible phosphorylation of creatine to creatine phosphate by ATP *(Bessman, 1985)*.

CK activity is greatest in striated muscles, brain and heart tissue. CK is inactivated by proteolysis in lymph, CK clearance is not affected by changes in heart rate, blood pressure or cardiac output. CK is not excreted in urine *(Clark et al., 1978)*.

There are three isoenzymes of creatine kinase, each composed of two subunits (M and B) that, in dimeric form, constitute the functional enzyme. CK-MM is found predominantly in striated muscle (skeletal and cardiac) *(Tsung and Tsung, 1986)*, CK-MB exist predominantly in the heart muscle (25-40% of CK activity) and also to a minor degree in skeletal muscle (<5%), and CK-BB in the brain, prostate, gut, lung, bladder, uterus, placenta and thyroid *(Payne et al., 1991)*.

With myocardial necrosis, total CK is detectable above the reference range 4 to 6 hours after the onset of ischemic symptoms. Total CK is not specific for cardiac muscle, however, and the normal reference interval vary by age, race, muscle mass, and sex *(Bias et al., 1982)*.

It may be elevated in a variety of pathological and other conditions. Therefore, CK alone has limited utility in the diagnosis of myocardial necrosis. All three of these isoenzymes species are found in the cell in the cytosol or associated with myofibrillar structures, however, there exists a fourth form that differs from others both immunolgically and by electrophoretic mobility. This isoenzyme, CK-Mt, is located between the inner and outer membranes of mitochondria and it constitutes in the heart up to 15% of total CK activity *(Payne et al., 1991)*.

Total plasma CK activity, although a highly sensitive index of infarction, is less specific, and may be elevated after a variety of conditions such as intramuscular injections, trauma, cardiac catheterization, surgery, cerebrovascular stroke, rhabdomyolysis or thyroiditis *(Puleo et al., 1990)*.

Electrocardioversion also causes significant elevation of total CK activity, but it doesn't elevate plasma CK-MB activity significantly unless the procedure is repeated several times *(Ehsani et al., 1976)*.

Creatine Kinase-MB:

Creatine kinase-MB (CK-MB) is the myocardial-specific isoenzyme of CK, composed of one M and one B subunit. It is found in small amounts in skeletal muscle, where further production can be induced by stress or injury *(Adams et al., 1993).*

CK-MB can be quantified by both activity and mass assays, although the latter is more sensitive and favored for early detection of myocardial necrosis. By mass assay, CK-MB is detectable above the reference range in the serum within 4 hours after the onset of ischemia and remains elevated for 24 to 36 hours. Because of its fairly rapid rise and fall, it can be used to detect reinfarction after an initial MI.

Like myoglobin and total CK, the use of CK-MB is limited somewhat in conditions resulting in skeletal muscle damage, because about 5% of skeletal muscle CK is of the MB isoform.

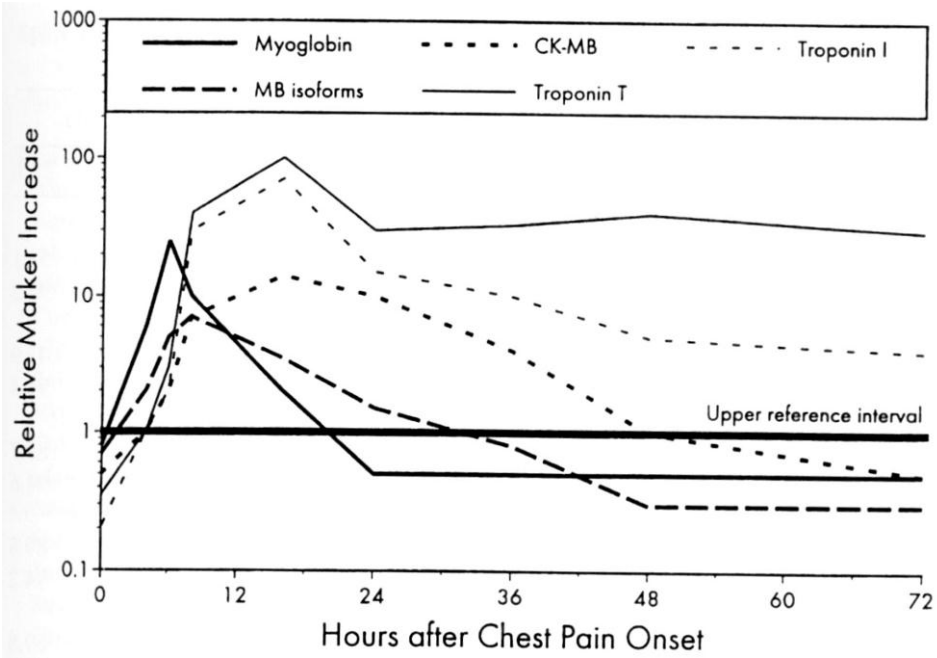


Figure (1): Time course after symptoms onset for various biochemical markers of myocardial necrosis. CK-MB= creatine kinase-MB isoenzyme.

CK-MB sub forms

Although four CK-MB isoforms can occur in the serum, CK-MB exists predominantly in two forms-MB2, the predominant form in tissue, and MB1, the seroconverted form. CK-MB is released as the MB2 subform at myocardial cell death and is converted in the serum by carboxy-

peptidase to MB1 through cleavage of the terminal lysine on the M subunit.

With acute myocardial necrosis, more MB2 is released than normal, increasing the amount of MB2 relative to MB1. When the ratio of MB2 to MB1 exceeds 1.5 and the absolute value for the MB2 sub fraction is ≥1.5 U/L, the finding is highly sensitive and specific for myocardial necrosis. Measurement of the sub forms has the ability to detect myocardial necrosis as early as 3 hours after symptom onset, important for emergency department use, and has an excellent negative predictive value *(Puleo et al., 1994)*.

In a study by *Zimmerman and colleagues*, CK-MB sub forms was also the most sensitive (91%) and specific (89%) of all marker assays for the early diagnosis of myocardial infarction in emergency department patients with chest pain within 6 hours from onset of symptoms *(Zimmerman et al., 1999).*

An elevated plasma CK-MB level is a diagnostic marker for myocardial infarction, associated with a very low incidence of false negative results if samples are appropriately frequently collected, and false positive results may occur since CK-MB can be released from tissues other than the heart (Fig.2) *(Roberts et al., 1975)*.

The MB component is increased in certain muscle disorders, particularly the Duchenne type of dystrophy and polymyositis *(Keshgegian and Feinberg, 1984)*.

Cardiac Troponin T

The troponins comprise a group of three proteins (C, I, and T), which interact with tropomyosin to form the troponin-tropomyosin complex. This complex is part of the regulatory and structural backbone of the contractile apparatus of striated muscle.

Troponin T is the 33-kDa structural component of the troponin complex that binds it to tropomyosin. Troponin T exists in three isoforms-skeletal (slow - and fast-twitch) muscle, and cardiac muscle.

During fetal development, the cardiac and skeletal forms are expressed in both skeletal and cardiac tissues. In the adult, the cardiac isoform is expressed only in cardiac muscle and the skeletal form only in skeletal muscle *(Adams et al., 1993)*.

Although there is evidence in the stressed human heart and in animal models that the skeletal muscle isoform may be reexpressed *(Anderson et al., 1991)*, the current assay for cardiac Tn T does not appear to react with this isoform *(Ricchiuti et al., 1998).*

The majority of troponin T in the myocyte exists bound in the troponin-tropomyosin complex; however, there is a small cytoplasmic pool of about 6% of the total.

Cardiac troponin T is detectable in the serum above the reference range as early as 4 to 6 hours after onset of symptoms of ischemia, probably reflecting early release of the cytoplasmic pool, and remains elevated for 10 days to 2 weeks as a result of slower and sustained release of troponin T bound in the troponin-tropomyosin complex.

Monoclonal antibodies can be used to differentiate the isoform of cardiac and skeletal muscle Tn-T. The immunoassay developed for this purpose is based on two anti-Tn T antibodies: M7, which is specific for cardiac Tn-T, and IB10 which binds to both heart and skeletal Tn-T. M7 confers specificity, while IB10 enhances the sensitivity of the test. A mixture of the antibodies is used in a one-step enzyme-linked immunosorbent assay (ELISA) *(Katus et al., 1992)*.

With available monoclonal antibody techniques, cardiac Tn T is not detectable in serum from normal volunteers. Because of the sensitivity of the assay compared with CK-MB (the current gold standard for diagnosis of acute MI), the specificity of cardiac Tn T for acute MI is lower, although, as will be detailed later in the

chapter, these "non-MI" elevations of cardiac Tn T in ACS patients appear to be prognostically important.

When the specificity of the assay was tested in healthy volunteers who underwent physical exercise no cross-reactivity was noted except in one patient who had a very severe skeletal muscle injury. In contrast, elevated CK-MB was detected in half of a similar group of healthy individuals. Several investigations have now confirmed this high level of specificity.

The prolonged elevated levels of Tn-T seen following A.M.I. result from it's continuous release by irreversibly damaged cardiomyocytes rather than because Tn-T has a prolonged serum half-life time.

In fact, Tn-T is relatively short lived with a half life of only two hours also the small amount present in plasma in the absence of infarction result in very low circulatory levels (undetectable <0.1 μg/ml) in normal volunteers, enhancing sensitivity of elevation for detection of infarction *(Bordor et al., 1992)*.

In the pathogenesis of ischemic myocardial injury, reversible as well as irreversible myocardial cell damage may occur. Myocardial cell damage that is limited to the cell membrane during ischemia results in only transient leakage of Tn-T from the cytosolic compartment.

In contrast, irreversible damage accompanied by the degradation of the contractile apparatus of the myofibrils leads to delayed and continuous release from the structurally-bound Tn-T compartment *(Senio et al., 1993)*.

In patients with A.M.I. two types of time course of biochemical marker Tn-T were noted.

In the patients with successful early reperfusion therapy for anterior M.I., coronary reperfusion was achieved 3.5 hours after the onset of M.I in correlation to the patients with late reperfusion therapy after inferior M.I. by PTCA which was performed, 13.5 hours after the onset. In both cases, the peak Tn-T concentration was about 35-fold higher than normal.

However, the release kinetics were entirely different. In the early reperfusion cases displayed a much more rapid increase in the first peak and a much smaller second peak than seen in the late reperfusion cases *(Senio et al., 1993)*.

Analysis of the Tn-T release kinetics suggest that the early rise in serum Tn-T is due to leakage from the cytosol of injured but still viable and washed-out myocytes. The later peak reflects irreversible damage to the contractile apparatus, namely infracted myofibrils. Second peak Tn-T corresponded wall to myocardial infarct size and left

ventricular function in the convalescent stage. In risk area for M.I. *(Senio et al., 1993)*.

Furthermore, release of cytosolic and compartmented Tn-T results in much extended time period of marker protein elevation in serum. This allows the detection of acute M.I. during a prolonged time interval which is not attainable by creatine kinase measurements *(Senio et al., 1993)*.

Thus cardiac Tn-T is a useful marker for the detection and monitoring of A.M.I. The release kinetics of Tn-T is related to both the structural and functional consequences of ischemic injury and the effects of reperfusion therapy. The early rise seems to be due to leakage from the cytosol of injured but viable myocytes. Whereas, the later peak reflects irreversible damage to the contractile apparatus *(Timmis, 1990)*.

The sensitivity of Tn-T for the prediction of cardiac events was 100% and its specificity was 57.1% *(Katus et al., 1991)*.

Table (1): Characteristics of various biochemical markers of myocardial necrosis.

	Myo-globin	Total CK	CK-MB (mass)	MB2/ MB1	cTnT	cTnI	LDH
Molecular weight (kDa)	17.8	85	85	NA	33	23.5	135
Cardiac-specific	No	No	++	++	+++	+++	No
Affected by renal function	Yes	No	Yes	No	Yes	Yes	No
Initial detection	1-3 h	4-8 h	3-4 h	3-4 h	4-6 h	4-6 h	8-12 h
Duration of elevation	18-24 h	12-24 h	24-36 h	Unknown	10-14 d	7-10 d	10 d
Rapid laboratory assay	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Bedside assay	Yes	Yes	Yes	No	Yes	Yes	No
Normal values	-	60-250 U/L	<30 U/L	-	<0.1ng/dL	<2ng/dL	200-450mg/dL

CK, creatinine kinase; cTnT, cardiac troponin T; cTnI, cardiac troponin I; LDH, lactate dehydrogenase; NA, not available; h. hours; d, days; ++, very specific; +++, extremely specific *(Topol et al., 1994).*

Cardiac Troponin I

Troponin I is a 23.5-kDa component of the troponin complex that inhibits the interaction of myosin cross-bridges with the actin/tropomyosin complex and thus regulates striated muscle contraction.

Like troponin T, troponin I exists in three isoforms, cardiac and skeletal (slow and fast-twitch), that are specific to the given tissue. Also similar to troponin T, troponin I exists predominantly bound within the troponin-troponin complex, but it also has a small cytoplasmic pool of about 2.5% of the total. Unlike troponin T, the cardiac form of troponin I is never expressed in skeletal muscle, even during fetal development *(Adams et al., 1993)*.

Troponin I is detectable in the serum slightly later than cTnT, about 6 hours after the onset of ischemia, and remains elevated for 7 to 10 days. Because of their long serum half-lives, neither cTnT nor cTnI is suitable for detection of reinfarction using currently available assays.

However, because they do remain elevated for days, they may be able to reveal an MI that occurred in days past (when presentation of the patient to medical attention is delayed, for example), when other markers of myocardial infarction have returned to normal.

In normal serum, at least 95% of the CK present is of the MM type and is probably largely the result of leakage from skeletal muscle, particularly during physical activity.

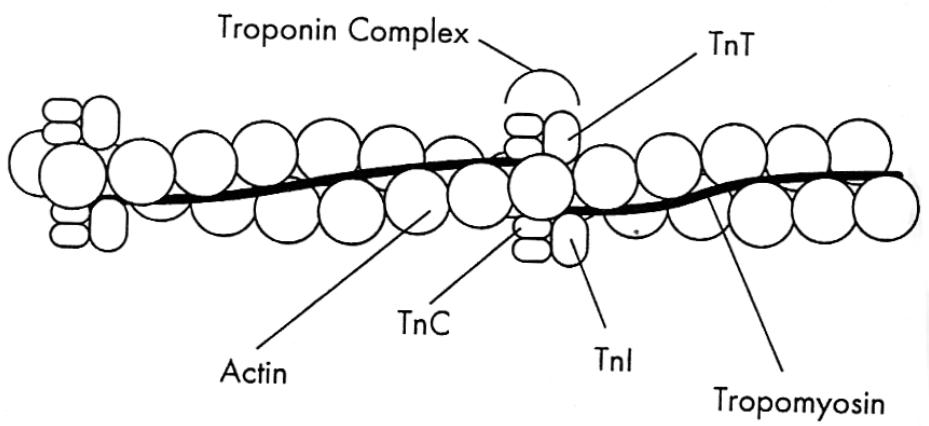


Figure (2): The troponin-tropomyosin complex. Tn T = troponin T; Tn C = troponin C; Tn I = troponin I *(Topol, 2001).*

Lactate dehydrogenase (LD):

LD is a tetramer composed of M (muscle, M.W. is 34 kDa and H (heart, M.W. is 34 kDa) subunits. The two subunits are encoded by different genes and give rise to 5 distinct isoenzymes that provide LD with an element of tissue specificity *(Marshall et al., 1991)*.

The molecular weight of the LD tetramer is approximately 135 kDa. LD-1 contains four H subunits, LD-2, three H subunits and one M subunit. LD-3, contains two H subunits and two M subunits and LD-5 four M subunits. LD is responsible for the interconversion of pyrurate and lactate as the final step in glycolysis *(Marshall et al., 1991)*. LD-1 is the predominant form in heart but also occurs in erythrocytes, brain, pancreas, kidney and stomach.

LD-2 is also abundant in the heart; LD-3, LD-4, and LD-5 are found in only trace amounts *(Wieland, 1961)*.

All LD isoenzymes are abundant in many tissues, whereas LD-5 is the predominant isoenzyme in the skeletal muscle, clearance of LD is via the reticuloendothelial system *(Smit et al., 1987)*.

Heart fatty acid binding proteins (H-FABS):

Heart fatty acid binding proteins (H-FABPs) are abundant cytosolic proteins of low molecular weight (M.W.

is 14 kDa) that are thought to be important intracellular fatty acid carrier proteins, three different FABPs are found in heart, liver and intestine, although each is also present in other tissues that use fatty acid as metabolic substrates.

H-FABPs have a unique structure and are abundant in myocardium, but detectable amount also are present in skeletal muscle and kidney. Serum H-FABPs is elevated after myocardial injury in rates, and serum and urine levels are elevated in humans after myocardial infraction. Initial and peak elevations occur earlier than increases in CK-MB consistent with the smaller size of H-FABPs *(Tanaka et al., 1991)*.

Coronary Arterial Anatomy as Viewed on Coronary Angiogram

It is important to gain an appreciation for the distribution of the coronary arteries in space as three dimensional objects from the two dimensional shadows cast on an image intensifier tube.

A brief review of the nomenclature of the views is needed. Each view is named for the position of the direction of the X-rays beam. The image intensifier views the heart from several positions. Therefore, the frontal means that the image tube is directly over the sternum. Left or right lateral refers to the image tube on the left or right side of the patient with the x-ray beam perpendicular to the frontal view.

Right anterior oblique places the image tube over the right side of the chest looking obliquely at the heart, while the left anterior oblique places the image tube over the left side of the chest. Cranial angulation refers to the location of the image tube in direction towards the head and caudal towards the feet *(King and Douglas., 1982).*

The Left Coronary Artery:

The left coronary orifice is located in the middle of the upper portion of the left coronary sinus. The left main artery travels left wards and slightly posterior for length

from 25 to 30 mm before dividing to two or three branches. Occasionally the left main artery is absent; with the anterior descending artery and circumflex artery arising from separate orifices but with no identifiable left main artery. A frontal projection will usually show the left coronary orifice and the left main segment to best advantage (Fig. 3).

Frontal view will not identify the portion of the left main artery that bifurcates. The left anterior oblique projection with steep cranial angulation will give additional views of the left main artery and shadow the area of bifurcation.

If the left main artery travels in a horizontal or slightly vertical direction, then foreshortening may limit the value of the left anterior oblique cranial view for the left main artery visualization. As the left main coronary artery curves around the pulmonary artery, it continues in the anterior interventricular sulcus as the left anterior descending branch.

The circumflex artery arises at the bifurcation, sometimes inscribe an acute angle with the left anterior descending artery and at other times inscribe a right angle with the LAD artery.

When the intermediate branch (the third branch) arises between the LAD artery and the circumflex artery

giving trifurcation of the left main, then this branch can be best visualized in the left anterior oblique view with significant cranial angulation. Both all frontal and right anterior oblique point obscures the origin of the three vessels.

Occasionally, in very horizontal hearts, a caudal angulation of the left anterior oblique view will provide a good view of the division of the left main into its more distal branches.

(King and Douglas., 1982)

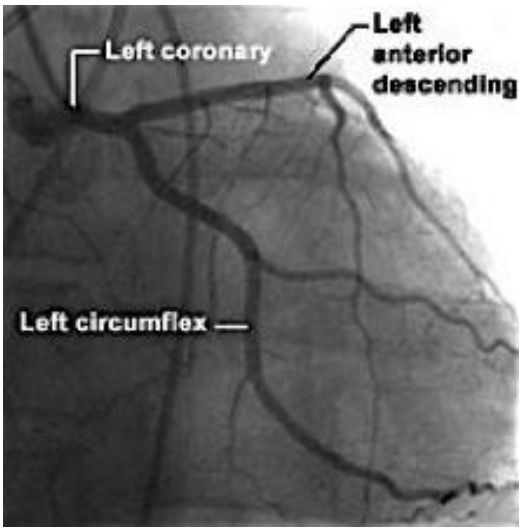


Figure (3): Coronary angiography, anterior view showing left coronary system **(Bairn and Grossman, 1996)**.

Left Anterior Descending Artery (LAD):

The left anterior descending artery continues to sweep in a gentle curve into the interventriaular groove

traveling toward the left ventricular apex when viewed in the right anterior oblique projection; the septal perforating branches can be seen traveling deep into the muscular septum.

The straight lateral view also gives an excellent image of the septal perforating branches as they take off at right angles from the anterior descending branch (LAD). In the left anterior oblique views, the septal vessels overlap with the LAD artery, and very little estimation of them could be made. These septal vessels differ from epicedial vessels in that they are straighter and move little with cardiac action, In contrast to the buckling of the epicardial arteries during systole (Fig.3).

In the 30º right anterior oblique view, the anterior descending artery is seen traveling inside the border of the heart by 1 to 2 cm. As it reaches the cardiac apex, the anterior descending artery continues around the apex and proceeds for a short distance up the inferior surface of the heart.

Occasionally, the anterior descending artery may terminate short distance from the apex in conjunction with a very long posterior descending branch of the right coronary artery that circles the apex and extends up the anterior portion of the ventricular groove.

(King and Douglas., 1982)

Diagonal Branches:

Diagonal arteries originate from the anterior descending artery and course over the anterior left ventricular free wall and appear on the lateral border of the heart when the heart is viewed in the right anterior oblique projection.

This shadow of the diagonal branch on the anterolateral tangent of the heart distinguishes it from the anterior descending artery, which travels inside the cardiac border toward the left ventricular apex.

In the right anterior oblique view, the LAD and the diagonal branches often overlap in their proximal portions. When viewed in the left anterior oblique projection, the diagonal branches could be seen clearly separated from the LAD.

Addition of cranial angulation to the left anterior oblique view will further enhance the ability to separate the origin of the diagonal branches and their extending course over the anterior left ventricular free wall.

(King and Douglas., 1982)

The Circumflex Artery:

Although the bifurcation of the LMCA is frequently thought of as a straight continuation of the LAD and a right angle take-off of the circumflex, the angles subtended by these two arteries vary from 30º to 180º. When this angle is wide, the right anterior oblique view gives good

visualization of the proximal circumflex artery, but when the angle is narrow, there is great overlap with the LAD in the right anterior oblique view (Fig.3).

These, the left anterior oblique view with cranial angulation remains an excellent view for the proximal portion of the circumflex artery, especially in cases with narrow angle. The addition of caudal angulation to the right anterior oblique view will improve visualization of the proximal circumflex artery without overlap.

In the right anterior oblique view, the circumflex artery travels away from the image intensifier as it courses in the atrioventricular groove. Because the right anterior oblique view is not an optimal view for the atrioventricular groove visualization, the circumflex foreshortening is visualized.

As the circumflex artery gives rise to marginal branches which travel in a direction perpendicular to the x-ray beam, and therefore are well visualized in all the right anterior oblique views. Take-offs of the marginal branches is usually obscured in the left anterior oblique views.

When the circumflex artery forms the dominant posterior circulation, the bifurcation of the posterior descending and the right ventricular branches is obscured in the right anterior oblique views, since those vessels are coming directly toward the image intensifier and are grossly foreshortened.

Addition of cranial angulation to the left anterior oblique views enhances the ability to see these posterior vessels. The posterior descending artery (PDA) arising from the circumflex artery is best seen in the right anterior oblique projection.

(King and Douglas, 1982)

The Right Coronary Artery (RCA):

The right coronary orifice is located in the right coronary sinus variably from the lower part to high near the Sino tubular ridge. It takes off anteriorly and about 30º to 40º to the right of the sagital plane (Fig.4).

The proximal part of the RCA travels in the epicardial fat in a more or less anterior direction, and then curves posteriorly into the atrioventricular groove on the right side. The proximal part of the right coronary artery varies greatly from an almost caudal direction, through a wide range of orientations, to an almost cranial direction.

After a short distance, however, the RCA turns in a direction posterior and caudal traveling in the right atrioventricular groove. It proceeds as a long conduit vessel changing little in it's diameter to reach the posterior portion. Conus artery, the first branch, frequently arises either as a separate orifice or from the very proximal portion of the RCA, and thus it is not frequently visualized by the selective right coronary injection .It courses medially around the pulmonary outflow tract at the level of the pulmonary valve.

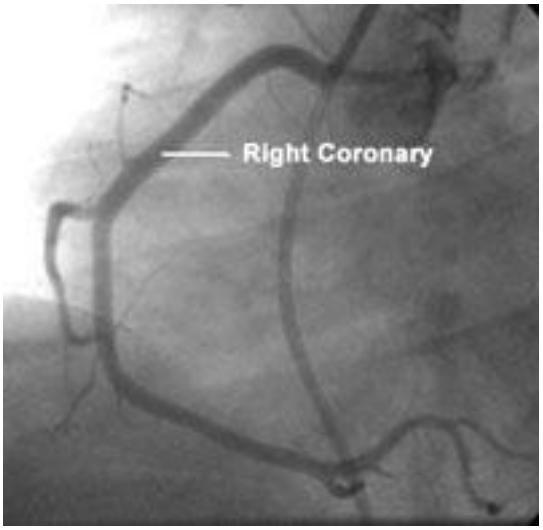


Figure (4): Coronary angiography, right oblique view showing the right coronary artery **(Bairn and Grossman, 1996)**.

Several other small right ventricular branches arise at right angles from the RCA and travel in a tortuous course over the right ventricular free wall. In about 55% of cases, the sinus node artery originates from the proximal portion of the RCA and travel atrially to reach the sinus node.

At the acute margin of the heart, there is usually a larger right ventricular branch which travels toward the apex of the heart. Occasionally, it supplies a significant portion of the interventricular septum especially the apical posterior portion.

The C-shape of the RCA could be best appreciated in the left anterior oblique view. This view usually gives an

excellent visualization of the RCA throughout its length until the posterior ventricular branches are reached.

The posterior descending artery (PDA) traveling on the image intensifier in the left anterior oblique views and therefore are greatly for shortened. Addition of cranial angulation to this view will improve visualization of the PDA considerably.

Right anterior oblique views will display the PDA perpendicular to the x-ray beam and will give excellent visualization of the vessel throughout its length. When there is a large left ventricular branch of the right coronary artery, that vessel may be superimposed on the posterior descending artery in the right anterior oblique view.

The addition of cranial angulation in the right anterior oblique view may separate these vessels. However, cranial angulation in the left anterior oblique view will best separate the origin of the posterior descending artery from the left ventricular branch.

The AV node artery consistently travels in a cranial direction from the u-turn of the right coronary artery at the crux. It can be identified radiographically as a single branch directed cranially and terminate as two short lateral branches in a T-configuration.

(King and Douglas, 1982)

When the left circumflex artery is the dominant posterior artery, the RCA usually bifurcates early into one branch traveling in the atrioventricular groove and another right ventricular branch of almost equal size.

The smooth tapering of these vessels and the small diameter of the proximal portion of the right coronary artery combined with the large posterior circulation considered as a non-dominant right coronary artery rather than totally occluded right coronary artery.

Overview:

One overriding consideration in the evaluation of the radiographic anatomy of the coronary circulation is the realization that the anatomy may be quite variable; however, all segments of the left ventricular myocardium are perfused adequately in the healthy heart.

Therefore , it is necessary to the surface coronary anatomy as seen in both the left coronary artery injections and the right coronary artery injections in order to form a special appreciation of the distribution of these vessels over the epicardial surface of the heart to ensure that all areas are served by adequate coronary circulation, then the possibility exists that occlusion of an artery is present or an anomalous origin of a coronary artery exists and that vessel have not yet been opacified.

(King and Douglas, 1982)

Percutaneous Transluminal Coronary Angioplasty (PTCA)

Historical Development:

The concept of percutaneous transluminal of coronary angioplasty to increase the luminal diameter by non surgical approach was first introduced by Drs. Dotter and Judkins in 1964 *(Dotter and Judkin, 1964)*.

They passed a series of stiff catheters through the atherosclerotic plaque in the iliofemoral artery from the percutaneous arterial access and showed improvement in the lumen caliber. Although this initial "Dottering" technique was successful in increasing the blood flow, it was not adopted by others owing to the bleeding complications at the entry site.

A decade later, Dr. Andreans Gruenzig in Zurich, Switzerland, improved the technique by attaching a small balloon at the end of the catheter. The balloon remains deflated until positioned at the site of atherosclerotic narrowing, where it was then inflated to increase the luminal diameter, this system reduced the overall bulkiness of the angioplasty equipment and bleeding complications at the arterial access site. This miniaturization also enabled the

catheter to be inserted into the smaller coronary arteries. Dr. Gruenzig initially tested the system in canine coronary arteries *(Gruenzig, 1976)*.

In human cadaveric vessels *Gruenzig et al., (1978)* performed the first clinical case of percutaneous transluminal coronary angioplasty (PTCA) with balloons to reduce atherosclerotic narrowing without the need for bypass surgery.

Since then, there has been an exponential increase in the number of PTCA performed (estimated to be more than 500,000 annually in the USA), resulting from improved operator skills and the PTCA equipment.

Although PTCA has performed well in most lesions, it was found to be associated with reduced procedural success and increased procedural complications in certain lesion subsets such as highly calcified, tortuous, completely occluded, or thrombus containing lesions and degenerated saphenous vein grafts *(Ryan, 1988)*.

To overcome these limitations, new angioplasty devices has been developed to improve the procedural success and reduce the complications. These have included atherectomy catheters that actually remove the atherosclerotic plaque material such as the directional coronary atherectomy, rotational atherectomy and transluminal extraction catheter,

laser catheter to ablate the plaque material, and metallic stents to scaffold the vessel *(Bittl, 1996)*.

The procedure:

The PTCA procedure requires high- resolution fluoroscopic equipment for angiographic visualization of the coronary arteries. The three main equipment components are a large lumen – guiding catheter (2-3), a flexible guide wire and the balloon catheter itself *(Landau et al., 1994)*.

Vascular access is obtained using the femoral approach in most cases, although other access sites such as the brachial or radial arteries can be used. The guiding catheter is advanced over a guide wire through the sheath into the ostium of the coronary artery to be treated.

Angiography of the diseased artery is performed to identify the site of the lesion, and then the flexible guide wire is carefully maneuvered across the stenotic lesion site and positioned distally. The deflated balloon catheter is then advanced over the guide wire.

Once the positions of the guiding catheter is engaged in the ostium, the guide wire is far distal to the lesion and the balloon is placed in the stenosis site which have been confirmed fluoroscopically, the balloon is inflated for 1 to 2 min – at 4 to 8 atm. with a mixture of saline and radio contrast so as to be visible fluoroscopically.

After the balloon is deflated and removed, the result is confirmed by injecting contrast material through the guiding catheter. If the angiographic results are suboptimal i.e. presence of more than 30% residual lumen stenosis or medial dissections, additional inflation was performed by the same or a bigger balloon, inflation pressures may vary according to on line fluoroscopic assessment of the lesion response and calcific lesions usually need high pressures.

During balloon inflation which results in transient occlusion of coronary blood flow, continuous monitoring of the electrocardiographic and homodynamic status of the patient is essential. Anginal symptoms are often provoked during the balloon inflation; however, they usually resolve spontaneously after balloon deflation.

When adequate angiographic results are achieved, the balloon and the guide wire are withdrawn from the artery and a final angiogram is obtained. Angiographic results are considered to be excellent if residual stenosis is less than 30% at the PTCA site compared with the adjacent normal reference segment.

If angiographic results are not optimal, or if abrupt or threatened closure or extensive dissection complicates the procedure, the angioplasty procedure should be complemented by intracoronary stent implantation to improve the PTCA

results and to prevent the acute procedural- related ischemic complications *(Dean et al., 2000)*.

Periprocedural antithrombotic medications include daily Aspirin (325mg/d), clopidogrel (300-600mg) before the intervention, followed by 75mg daily and heparin (100 to 150U/kg initial bolus with additional boluses adjusted to maintain the activated clotting time (ACT) at around 300 sec., to prevent platelets deposition and thrombin-mediated fibrin formation at the PTCA site *(Popma et al., 2001).*

Heparin administration is often terminated after the procedure, but may be continued for up to an additional 12 to 24hs if the procedure has been complicated by dissection or thrombosis, or if the patient has been clinically unstable.

The arterial sheath is removed when the anti-coagulant effect of heparin is resolving, as manifested by an ACT of less than 150sec. Manual pressure or device-based compression or both of the puncture sites is essential to achieve adequate homeostasis. Discharge after successful procedure varies according to the clinical sinario before, during, and after the PTCA, ranging from discharge the next day to few days of hospitalization of unstable patients.

Indications and contraindication:

The indications for PTCA have been evolved over years. Initially, mostly because of the limitations of the angioplasty equipment, PTCA was limited to proximal

lesions in rather straight segments and usually in single vessel coronary artery disease. Unlike coronary artery by pass surgery (CABG), PTCA has been applied empirically to treat any flow-limiting coronary artery lesions. *(Farisi et al., 1999).*

Because of continuing increase in operator experience, improved coronary angioplasty has recently broadened dramatically. Currently accepted indications for PTCA are based on angiographic findings of significant stenosis in one or more major epicardial arteries, which perfuse at least a moderate-sized area of viable myocardium, in selected patients.

Indications:

- Angina refractory to medical therapy.
- Recurrent ischemic episodes after myocardial infraction or major ventricular arrhythmia.
- Clear evidence of myocardial ischemia on resting ambulatory or exercise ECG.
- Objective evidence of myocardial ischemic, which increases the over all risk for noncardiac surgery.
- Acute MI, with obstructed severely stenosed infract-related coronary artery *(Ryan, 1988).*

Contra indications:

- High risk anatomy, including significant left main disease, which would most likely cause homodynamic compromise with vessel closure.
- Severe, diffuse, extensive CAD better treated surgically.
- Target lesion morphology with very low anticipated success rate, unless PTCA is the only reasonable treatment.
- No coronary stenosis greater than 50% diameter reduction.
- No objective clinical evidence of myocardial ischemia.
- Absence of on-site surgical backup, qualified PTCA operator, and adequate radio-graphic imaging *(Ryan, 1988)*.

Mechanism of Arterial Dilatation by PTCA:

PTCA increases the size of the arterial lumen by barotraumas, with endothelial denudation, cracking, splitting, and disruption of the atherosclerotic plaque *(Faxon et al., 1982)*.

Dehiscence of the intimae and plaque from the underlying media and stretching or tearing the media and adventitia were noted in animals, human, and neuropathy studies *(Farb et al., 1990)*.

The presence of intimal flap dissections has been observed in 50 to 80 % of successfully treated patients using intracoronary ultrasound imaging *(Potkin et al., 1992).*

These morphologic alterations open up the coronary artery for blood flow, leading to increased lumen size and improvement of coronary flow reserve.

Oversized or uncontrolled balloon dilatation may be deleterious, causing extensive dissection, plaque hemorrhage, and thrombus formation, with ensuing abrupt closure of the artery at the treatment site. The peri-procedural use of heparin and Aspirin may reduce these complications.

The acute traumatic effect of PTCA is eventually replaced by arterial healing response with reendo-thelialization, resulting in chronic arterial dilatation (arterial remodeling) with sustained lumen patency.

Nevertheless, in about 30 to 50 % of treated patients, renarrowing of the PTCA site occurs usually in the first 6 months after the procedure owing to the combined effects of arterial shrinkage and proliferation of neointemal tissue at the original treatment site *(Mintz et al., 1996)*.

Limitations of the PTCA:

Angioplasty has had many limitations. The first consists of procedural complications, especially vessel dissections and abrupt closure. The second is restenosis, occurring usually within the first 6 months after a successful angioplasty procedure in certain complete lesion subsets, such as very long, diffuse lesions and chronic total occlusions *(Lincoff et al, 1992)*.

Percutaneous Transluminal Coronary Angioplasty Complications

From 1950 through the 1970's essentially all cardiac catheterizations were performed to evaluate individual disease states to guide medical therapy or to provide a road map for cardiac repair. In the 1980's however, cardiac catheterization began to play an increasingly important role in treating as well as diagnosing cardiovascular lesions.

In the 1990's however, cardiac application of catheterization based treatment has become known as "interventional cardiology" which may involve delivery of mechanical, thermal, microsurgical or light energy to cardiovascular lesions by means of specialized percutaneously inserted catheters with improved equipment and an increasing number of experienced operators.

The primary success rate of PTCA has improved over the past 10 years, and the number of procedures performed has risen rapidly thus, PTCA is playing an increasingly important role in the treatment of chronic stable angina *(Wong et al., 1990; Ellis et al., 1991).*

Minor complications following coronary angioplasty are in many ways similar to those associated with routine cardiac catheterization, but some are peculiar to the

procedure of angioplasty itself. The most comprehensive reviews of minor complications after coronary angioplasty is that of *Bredlau et al. (1985)* who reviewed 3500 consecutive angioplasty procedures, six percent of patients experienced an isolated minor complication. Side branch closure and ventricular arrhythmias were seen.

Acute procedural complications:

Abrupt vessel closure:

Acute procedural complications, such as abrupt closure of the coronary artery after PTCA, are associated with increased morbidity and mortality. Over all, the risk of periprocedural myocardial infarction (MI) during PTCA is 3 to 5%, the risk of death is about 1%. Extensive coronary dissection or coronary thrombosis or both have been often associated with such deleterious events *(Tenaglia et al., 1994).*

Other acute complications of PTCA include coronary perforation, vessel rupture, and distal embolization with slow or no flow phenomenon (usually found in saphenous vein graft intervention).

Abrupt vessel closure occurs in 2 to 8% of patients undergoing PTCA, usually within minutes after the coronary intervention while the patient is still in catheterization laboratory. In about 25% of patients,

however, abrupt vessel closure is delayed up to 24 hrs after the procedure.

The mechanisms of abrupt PTCA induced vessel closure include extensive dissections and coronary vasospasm. The recognition, of extensive dissections is crucial, because it is associated with major ischemic complications if untreated.

A thrombus formation is most likely to occur in patients with extensive dissections, owing to exposure of thrombogenic arterial wall elements to obstructed blood at the dissection site.

Several risk factors for abrupt vessel closure have been identified:

Risk factors for abrupt vessel closure after PTCA:

- Female gender.
- Unstable angina.
- Multivessel coronary artery disease.
- Angiographic morphology of intra coronary thrombosis prior to intervention.
- Diffuse (>10 mm), eccentric calcified, or branched lesion morphology.
- Procedural extensive dissection.
- Use of oversized balloons for inflation.

The best treatment for abrupt arterial closure is immediate coronary stenting, which was shown to be effective in restoring antegrade coronary flow and reducing the need for emergent bypass surgery(Lincoff, et al, 1992).

Hypotension:

Hypotension following PTCA is common but should be vigorously investigated and treated because hypotension from any cause may decrease coronary blood flow and provoke thrombotic closure of a recently dilated artery.

Patients returning to their hospital beds after angioplasty who are placed on standard does of topical nitrates and calcium channel blockers often have systolic blood pressures between 90 and 120 mmHg. Symptomatic hypotension may result from myocardial ischemia, cardiac tamponade, groin, gastrointestinal or retroperitoneal bleeding or dehydration because of limited oral fluids intake, diuretic, contrast-induced osmotic diuresis or simply standing up abruptly after prolonged bed rest.

Dehydration-related hypotension is prevented best by allowing the patient who is scheduled for an afternoon procedure to have a light liquid breakfast and by the routine administration of at least 2L of intravenous fluid over the first 8 to 12 hours after the patient's return to his or her room *(Lang, 2005).*

Ventricular arrhythmias:

Ventricular arrhythmias requiring cardioversion were noted in 1.5% of patients (*Bredlau et al., 1985)* and 1.8% of patients in more recent series studied by *Lembo et al. (2005).* Serious ventricular arrhythmias generally occur in one of few situations. Excess dye injection, particularly into the right coronary artery, may itself cause ventricular fibrillation.

Ventricular fibrillation also may occur if dye is allowed to remain static in the coronary tree, as may occur with guide catheter wedging or prolonged balloon inflations. These complications should decrease as operator experience is gained *(Kennedy, 1982).*

Complex premature ventricular contractions and occasional nonsustained ventricular tachycardia are seen after perhaps 2-3% of apparently uncomplicated angioplasty procedures. These arrhythmias usually abate over 12-36 hours and do not, in general, require treatment *(Bredlau et al., 1985).*

New conduction defects:

New conduction defects were noted in 0.9% of patients *(Bredlau et al., 1985)*, right bundle branch block was by far the most common, followed by first-degree atrio-ventricular block. These defects almost always discharge,

but occasionally required the elimination of Diltiazem or other drugs that depress cardiac electrical activity *(Kennedy, 1982).*

Femoral artery complications:

Femoral artery complications, such as pseudo-aneurysm formation or large hematoma formation requiring surgical repair, were noted in 0.6% of patients and seem to be increasing with larger sheath use and more anticoagulation *(Bredlau et al., 1985)*. These complications occurred much more commonly in females over the age of 70 year, diabetics, and the obese *(Meier, 1998).*

Early sheath removal that is 2 to 4 hours after the completion of the procedure when the activated clotting time falls below 170 seconds followed by bed rest for 8 to 12 hours and careful ambulation has not been associated with an increase in complications in patients with a good PTCA result and greatly decreases the discomfort of prolonged bed rest *(Green et al., 1985).*

Longer periods of strict bed rest (up to 36 hours) appear to be helpful with stent patients, as postangioplasty decrements of 3 gram or more of hemoglobin were found in 6% of patients after PTCA in a prospective study by *Alderman et al., (1987).*

This decrement, of course may be due to blood loss during the procedure, or on occasion, to hemodilution after it. Decreases in hemoglobin level have related to heparin use and partial thromboplastine times of greater than 60 seconds and are seen more often in the elderly. However, transfusion was required in less than 0.5% of patients *(Bredlau et al., 1985).*

Coronary emboli:

Clinically important coronary emboli are unusual *(Falk and Boris, 1985),* except when dilatation is performed in the presence of a thrombus or diffusely diseased saphenous vein bypass graft *(Aeron et al., 2001).*

Emboli in the setting of elective native vessel PTCA occur in less than 1 in 500 procedures. This rare complication occurs most commonly with over rotation of the guide wire when the distal end is entrapped in a total or high grade stenosis, but occasionally an isolated component failure caused by design and production flows has contributed to its occurrence *(Hartzler et al., 1987).*

Hartzler's group in 1987 advocated removal of the retained guide wire fragments which extends into a proximal coronary vessel or the aortic root. The American Heart Institute group reported 3 patients with chronically retained intracoronary guide wire fragments who had no

clinical events during follow up ranging from 6 to 60 months.

A pathological study in animal model has demonstrated that PTCA produces endothelial desquamation or splitting of the fibrous cap of the atherosclerotic plaque *(Block et al., 1982).*

The demonstration of endothelial desquamation and intimal splitting implies that there is peripheral embolization of fragments of endothelial cells or endothelial patches, and that the contents of the atherosclerotic plaque may be released at the time of PTCA *(Block et al., 1982).*

Less than 5% of patients who undergo PTCA develop evidence of ischemia without demonstrated occlusive changes on repeat coronary angiography *(Block, 1982).*

One might speculate that these patients may have had distal coronary embolization of endothelial fragments and cholesterol plates, which produce subendocardial ischemia and infraction.

Transluminal angioplasty produces desquamation of endothelium with exposure of subendothelial microfibrils and subsequent platelets adhesion in the area of angioplasty, thus, small platelets microemboli may also contribute the chest pain present in some patients after angioplasty.

Therefore, micro-embolization of endothelial fragments, cholesterol plates or platelets thrombi may account for some the episodes of ongoing pain of coronary insufficiency after successful PTCA *(Dorros and Spring, 1980).*

Embolization of thrombotic or atheromatous material probably occurs more frequently after balloon angioplasty of coronary arteries than has been recognized yet it is clinically asymptomatic in most cases because of the small size and number of emboli *(Lee, 1980).*

Distal embolization during PTCA for chronic total occlusion:

Distal embolization represents occasional and mostly blind complication of recanalization attempts of a chronically total occluded coronary artery which may cause a limited infraction *(Kereiakes et al., 2003).*

Distal embolization after recently advanced techniques:

a- Directional coronary atherectomy (DCA):

Angiographic distal embolization caused by excised tissue or thrombus is a rather rare complication in native coronary arteries *(Safian et al., 1990).*

b- Rotational atherectomy:

In rotational atherectomy for branch osteal lesions there is a potential risk for embolization of debris down the

uninvolved artery; this can lead to "no reflow" phenomena with resultant serious ischemia *(Goudreau et al., 1993).*

c- Transluminal extraction atherectomy (TEC):

Working on TEC in saphenous vein grafts reported, 11.3% of distal embolization which was associated with higher rates of both minor and major complication *(Hong et al., 1994)*.

Cardiac tamponade:

Cardiac tamponade during or after PTCA is seen almost exclusively when the operator is overly vigorous in placing a temporary pacing catheter into the right ventricle, although coronary perforation leading to tamponade seems to be more common with alternative technologies (excimer and infracted Laser, rotational and extraction atherectomy) *(Ellis et al., 1992).*

Tamponade is probably more often seen in elderly females and may by causing a fall in blood pressure; induce acute closure of the dilated vessel. For this reason and because atropine-resistant bradyarrhythmias, it is now recommended that pacing catheters be placed into the right ventricle only for patients with high risk lesions or pre-existent bifascicular block *(Goldbaum et al., 1985).*

Coronary Restenosis:

Restenosis after successful coronary angioplasty, usually occurs within the first 6 months, continues to be

the major limitation of this procedure and a therapeutic challenge. Recent randomized studies still show 32 to 57% angiographic restenosis rates after PTCA *(Hong et al., 1997)*.

There have been numerous randomized studies with various classes' pharmacologic agents in an effort to reduce the rate of restenosis. Most of these studies intended to reduce neointemal hyperplasia, but failed to reduce restenosis. Likewise, randomized studies with new angioplasty devices, such as directional coronary atherectomy (DCA), showed no reduction in restenosis *(Hong et al., 1997)*.

However, the stent restenosis study (STRESS*)* *(Fischman et al. 1994)* and the Belgium-Netherlands stents study (BENESTENT) *(Serruys et al., 1994)* documented the efficacy of the palmaz-schatz tubular slotted stents in reducing restenosis compared with that which occurred with PTCA in focal lesions located in native coronary arteries.

Revising several clinical studies, serial intravascular ultrasound (IVUS) observations suggest possible explanations for the efficacy of stents and lack of effect with other angioplasty devices, and pharmacologic agents aimed primarily to blunt cellular proliferation *(Mintz et al., 1996).*

These studies suggest that the predominant mechanism of restenosis after Non- stent PTCA procedures is chronic negative geometric remodeling of the treatment

site. This results in constriction of the vessel wall rather than excessive neointemal hyperplasia causing lumen compromise.

Several predictors of procedural failure in chronic total occlusions are identified;

- Occlusions in 75% or more of the vessel lumen for >3 months versus occlusions in 35% for <2 months.
- Absence of any antegrade flow through the occlusion (50 % versus 77% with tapered occlusion)
- presence of bridging collateral vessels (23 %versus 71%), and
- Lesion > 15 mm in length.

Multiple nonrandomized series of repeat PTCA for treating restenotic lesions after the original PTCA have found the second PTCA to be safer with higher procedural success *(Dimas et al., 1992).*

The successful second PTCA seems to produce similar restenosis rate as the first PTCA. Other groups have evaluated the safety and efficacy of a third PTCA for treatment of a second restenosis.

Although the procedure can be performed safely with a high probability of acute success, the restenosis rate appear to be markedly higher (40%), especially if the interval between the second and third PTCA, is less than 3 months *(Tan et al., 1995).* For these patients, more

definitive therapy, such as implantation of coronary stents, is warranted *(Colombo et al., 1996).*

A randomized study (REST) compared the Palmaz-schatz stents with PTCA in native restenotic lesions and found a markedly reduced second restenosis rate (11.7 % compared with 37%) in the stent group *(Erbel et al., 1998)*.

Complex Coronary interventions:

The treatment of diffuse coronary lesions has been identified as a factor adversely influencing both acute and long-term success rates in most reported PTCA and new angioplasty devices studies. Experiences with the treatment of diffuse lesions were associated with increased risk for acute complications (5% up to 10 %) and late restenosis 50% in most of studies *(Sharma et al., 1993).*

Likewise, the treatment of chronic total occlusion (CTO) remains a major challenge for PTCA, with relatively low procedural success rate and high incidence of restenosis and late reocclusion *(Puma et al., 1995)*.

Successful recanalization is achieved in approximately 65% of attempted procedures. Inability to cross the stenosis with a guide wire is the most common cause of procedural failure. Long- term success is also limited, and restenosis is expected in more than 50% of patents.

A recent randomized trial has shown that stent implantation for chronic total occlusion (CTO) can significantly reduce the occurrence of clinical and angiographic restenosis and reocclusion after successful recanalization. Thus, stent implantation has become a common clinical practice in most catheterization laboratories after CTO recanalization *(Sirnes et al., 1996)*.

Patients and Methods

This prospective study included 90 consecutive patients with chronic stable angina pectoris and critical stenosis of the LAD coronary artery (>90%) diagnosed by a previous coronary angiography, who underwent coronary intervention in cardiac catheterization laboratory at Ibn Sena Hospital and Benha University Hospital during the period from March 2007 to September 2007.

Inclusion criteria:

- Stable angina: angina without changes in frequency or pattern for 6 weeks before the intervention.
- Patients with myocardial infarction (more than 2 weeks).

Exclusion criteria

Patients who were known to suffer from the following diseases were excluded,

- Uncontrolled hypertension.
- Uncontrolled diabetes mellitus (whether type I or type II).
- Congestive heart failure or valvular heart disease.
- Acute coronary syndrome i.e. patients suffering from unstable angina or myocardial infarction within the last two weeks.

- Advanced kidney and liver diseases.
- Baseline elevation of cardiac troponin I and cardiac troponin T i.e. preprocedural troponin I >2 ng/ml, or troponin T >0.1 ng/ml.
- Unsuccessful PTCA or PTCA followed by complication.

All patients were planned for

I- History taking:

Proper history taking i.e. personal history e.g. smoking, hypertension, diabetes mellitus …etc and family history for coronary artery diseases.

II- Clinical examination :

- Proper general examination by blood pressure, pulse, neck veins and lower limbs.
- Proper local examination by abdominal, chest and cardiac examination.

III- Electrocardiography monitoring (ECG):

- A 12 leads ECG is recorded the day before the PTCA
- During the procedure, 3 ECG leads were constantly monitored.

Occurrence, severity, and duration of chest pain, and acute ST segment elevation or depression (> 0.1 mV) and T-wave abnormalities were recorded.

IV- Echocardiography assessment:

Before the Percutaneous coronary intervention (P.C.I.), all patients were assembled for echocardiography assessment of the left ventricular systolic function i.e. ejection fraction and left ventricular dimentions.

After 6 months of the PCI echo was done for every patient to reevaluate the effect of coronary revascularization on the global systolic function of the left ventricle, end systolic and end diastolic dimentions.

V- Periprocedural Cardiac troponin I and T assessment:

Blood samples were collected just before the PCI at base line then 12 hours and 24 hours latter as follows;

(a) Blood sampling:

Blood samples were taken from the femoral sheath into dry sterile tubes without anti-coagulants and covered, Patient name, serial number and serial collection time were registered on the tube then kept in room temperature (at 25c) for 20 minutes to allow clotting and samples were centrifuged at 3000 g for 10 minutes then serum collected and stored in aliquots at 0°C in refrigerators until analysis.

(b) Analytical method:

Biochemical analysis was performed by biochemists unaware of patients' histories for quantitative analysis of cardiac troponin I and T. An enzyme linked immunosrbent assay (ELISA) was used by the UBI MAGIWEL troponin I quantitative CD-101 materials (normal value <2ng\ml). This assay showed no cross reactivity with skeletal muscle troponin I or other cardiac troponins. Boehringer Mannheim corporation materials for troponin T analysis (normal value <0.1 ng/ml) was used *(Apple, 1999)*.

VI- The percutaneous coronary intervention (PCI):

- Pre-intervention coronary angiography was done for all patients and angiographic analysis and measurements were performed in at least two orthogonal angiographic projections.
- Quantitative measurements of the target lesion was performed before the intervention by measurement of lesion length, minimal luminal diameter (MLD), and percent diameter stenosis (DS %).
- The type of lesion according to lesion morphology:

  Type A lesion, concentric, non-angulated, no calcifications and <10 mm length.

  Type B lesion, eccentric, moderately angulated with moderate calcification and ranged between 10-20 mm.

Type C lesion, diffuse excessive tourciousity and length >20 mm (*Sharma, et al, 1993*).

The PCI procedure was done using standard techniques i.e.

- Routine patient care before and after the intervention including pre-treatment with aspirin (300mg) and clopidogrel (plavix 300 mg) followed by 75 mg daily dose for 12 months.
- I.V. heparin (10.000 to 15.000 IU) administered at the beginning of the intervention and followed by additional boluses as needed to maintain the activated partial thrombo-plastine time (a PTT) double that of control value throughout the procedure.
- An appropriate guiding catheter (from 6-8 Fr) was introduced retrogradly via the standard femoral approach.
- Attempts to cross the stenosis were initially made with 0.014 inch guide wire, progressing from flexible to stiffer wires, preferring stiffer wires for diffuse lesions.
- When the guide wire was confirmed to be intraluminal, it's tip advanced as far distal as possible down the vessel and the deflated balloon was advanced over the wire across the lesion then serial inflations were performed up the nominal pressures or more in order to achieve full expansion, then the balloon was deflated and

removed, then the stent was advanced over the guide wire across the lesion and proper apposition.

- The procedure was considered successful when the residual stenosis in the dilated segment was less than 20% in two orthogonal views as associated with quantitative analysis *(Saadeddin et al., 2002)*.
- Post procedural angiography of the treated lesions was observed by serial angiography in at least two perpendicular projections to exclude any complications as dissection, intraluminal thrombosis, distal embolization, and slow or no reflow. Patients were then transferred to coronary care unit (CCU) for cardiac monitoring at least 24 hrs after the PCI and stent implantation.
- Patients were classified into two groups:

- **Group A:** patients who underwent balloon dilatation and stents implantation.
- **Group B:** patients who underwent balloon dilatation only, then

- Predictors of cardiac troponin I were discussed.
- Clinical follow up end points: patients were followed up for 6 months after the end of the procedure, and they were questioned for the recurrence or presence of cardiovascular symptoms (angina, MI), hospitalization

or need to repeat coronary revascularization. The families of patients were contacted to determine the cause of death.

- Follow up during the early in hospital phase was accomplished by daily review of medical records.
- All patients were followed up for 6 months after the discharge in the outpatient cardio-clinics and the adverse cardiac events were recorded i.e. recurrent angina pectoris, recurrent MI, death and need for coronary revascularization.

Informations were collected by review of patients' ongoing medical records, documentations of re-admission to coronary care units (CCU) and by contact with other physicians and hospitals.

The end points of the follow up were:

1. Death due to cardiac cause.
2. Recent ischemia defined as one or more of the following end points (rest angina, MI, hospitalization for acute coronary events).
3. Revascularization procedure.

Patients with any of the end points were interviewed and their medical reports were reviewed.

Statistical Analysis:

All data were collected, verified, and revised then, continuous normally distributed variables expressed as mean value ± SD and categorical variables expressed as numbers and percentage where:

$$\text{mean} = \frac{\sum x}{n}$$

where $\sum$ = sum &

n = number of observations

Standard deviation (SD):

$$= \sqrt{\frac{\sum [X_1 - X_2]^2}{n-1}}$$

where:

X_1 = mean of the first group
X_2 = mean of the second group

Comparison between the groups was made by student t-test for continuous variables and Chi-square test for categorical variables.

Student t-test:

$$\frac{X_1 - X_2}{\sqrt{SE_1 - SE_2}}$$

where:

SE_1 = standard error of the first group
SE_2 = standard error of the second group

Bivariate correlations were analyzed by Spearman's test if indicates.

Comparison between the results of testing procedures in different groups of patients expressed as a two sided P-value.

where:

A P-value of less than 0.05 was considered to indicate statistical significance.

A P-value of less than 0.01 was considered to indicate high statistical significance.

but A P-value of more than 0.05 indicate no statistical significance.

Clinical predictors of post catheter cardiac Tn-I elevation were determined using a patient based analysis *(Sendecor and Cochron, 1980)*.

Results

(A) Demographic data:

I. Patients' criteria:

A total of 90 patients were known to be treated from chronic stable angina and diagnosed by previous coronary angiography having significant proximal left anterior descending artery (LAD) lesion >90% were enrolled in this study.

All patients underwent elective percutaneous transluminal coronary angioplasty (PTCA) to the proximal left anterior descending artery (LAD), in addition elective stenting were done in 66 (73.33%) patients.

Patients were divided into two groups:

Group A: 66 (73.33%) of patients underwent balloon dilatation and stents implantation.

Group B: 24 (26.77%) of patients underwent balloon dilatation only.

Eighty four (93.33%) of patients were males, 62(93.33%) of them in group A, while, 22 (91.67%) patients from group B, 6(6.67%) of patients were females, 4(6.06%) of them in group A, while, 2(8.33%) patients in group B. their ages ranged between 41 and 65 years with mean age 50.0 $\pm$ 4.47 years.

Thirty six (40%) patients were hypertensive, 27(40.91%) of them in group A, and 9(37.5%) patients in group B, also, 18(20%) patients were diabetic, 13(19.7%) of them in group A and 5(20.83%) patients in group B.

Forty two (46.67%) of patients were smoker, 29(43.94%) of them in group A and 13(54.17%) patients in group B, also, 21(23.33%) patients were obese, 15(22.73%) of them in group A and 6(25%) patients in group B.

Fifty one (56.67%) of patients had increased total serum cholesterol level, 36 (54.55%) of them in group A and 15(62.5%) patients in group B, and also 27 (30%) patients had positive family history of coronary artery disease, 17(25.76%) of them in group A and 10(41.67%) patients in group B (Table 2).

Table (2): Demographic data of the patients.

Character		Group A n=66	Group B n=24	P-value
Sex	Males	62(93.93%)	22(91.67%)	>0.05
	Females	4(6.07%)	2(8.33%)	
Age (mean ±SD)		49.77±4.17	51.12±4.2	>0.05
Risk Factors				
Hypertension		27(40.91%)	9(37.5%)	>0.05
Diabetes mellitus		13(19.7%)	5(20.83%)	>0.05
Smoking		29(43.93%)	13(54.17%)	>0.05
Obesity		15(22.73%)	6(25%)	>0.05
Hypercholesterolemia		36(54.55%)	15(62.5%)	>0.05
Positive Family history		17(25.76%)	10(41.67%)	>0.05

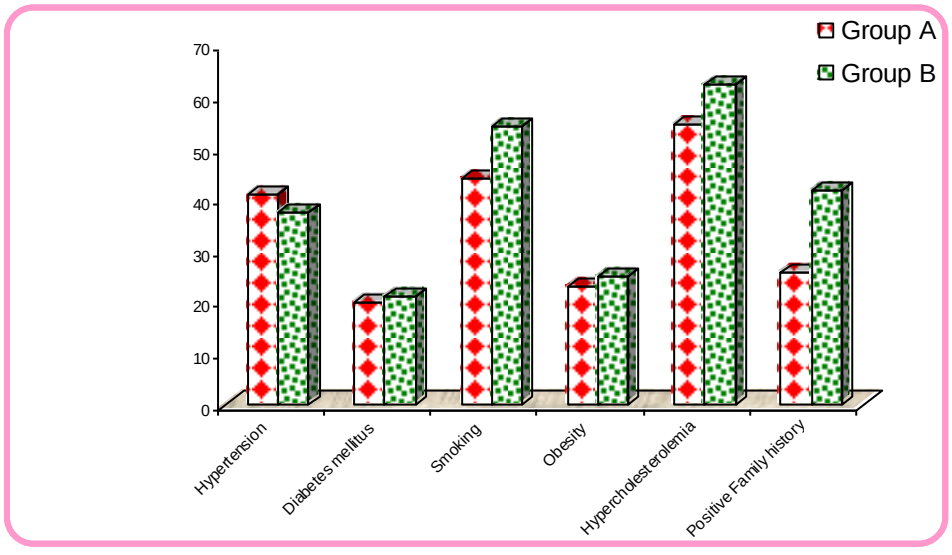


Fig. (5): Demographic data of the patients.

II. Electrocardiography (ECG):

During admission, ECGs showed pathological Q-waves in 18 (20%) of patients, ST-T waves changes in 54 (60%) of patients. While, ECGs performed after the intervention showed new ST-T waves changes in 36 (40%) of patients, 9 (27.27%) of them with old anterior MI showed T-waves inversion in anterior leads, 3 (9%) of them showed ST-segment depression and 2 (6%) of them showed ST-segment elevation but 19 (57.85%) of them showed normalized ST-T waves, and 3 (3.33%) of patients with preliminary normal ECG showed ST segment elevation in anterior leads.

III. Echocardiography:

ECHOs were done for all patients before the coronary intervention, and six months latter, the global myocardial function and dimentions were studied.

Table (3): Lesion related Quantitative coronary angiography measurements.

Parameter	Group A	Group B	P-value
	n=66	n=24	
Lesion Length	27.7±6.3	27.1±6.93	>0.05
Pre-catheter MLD (mm)	4.45±3.64	5.25±2.31	>0.05
Pre-Catheter DS(%)	7.55±3.64	8.6±2.02	>0.05
Post-catheter MLD (mm)	7.42±2.25	6.82±2.68	>0.05
Post-Catheter DS(%)	11.22±2.26	11.65±1.86	>0.05

(B) Quantitative angiographic analysis of lesion related QCA measurements:

All patients had proximal left anterior descending artery (LAD) lesions more than 90%. There were no significant differences in lesion length in the studied groups. Also, pre and post catheter minimal luminal dimensions, distance of stenosis percent cleared no significant differences in the studied groups (Table 3).

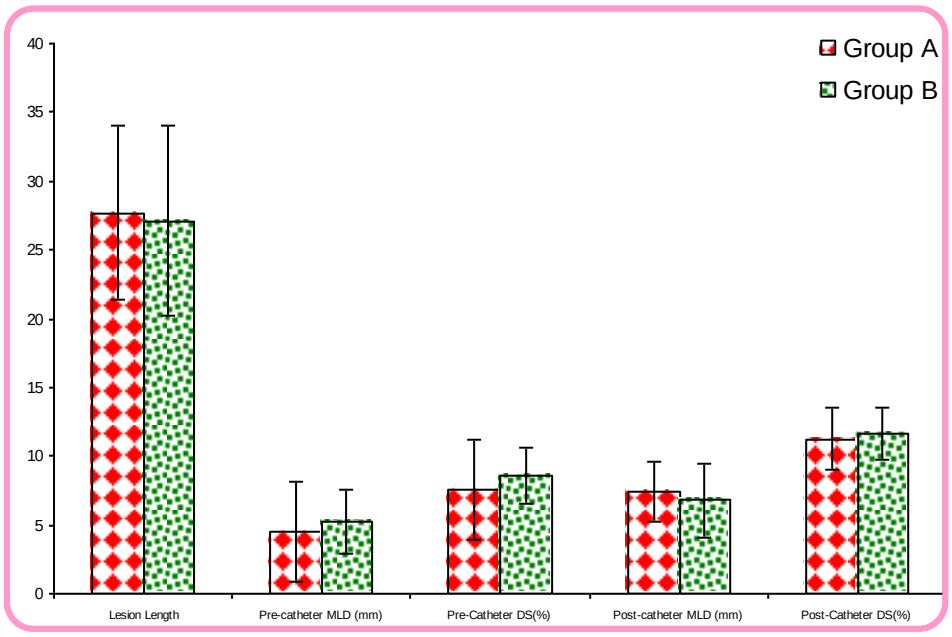


Fig. (6): Lesion related QCA measurements.

(C) Procedural data:

The mean procedural duration was 1.2 ± 0.33 hrs.

I. Balloon parameters:

Balloon diameters ranged between 2 and 3.5 mm, inflation pressure of the balloon ranged between 10 and 28

atm. and total time of inflations ranged between 1.5 and 4.5 minutes.

II. Stents parameters:

Sixty six baremetal stents were implanted, the diameter ranged between 2 and 3.75 mm, stents' lengths ranged between 12 and 28 mm and inflation pressure of stents ranged between 10 and 30 atm.

(D) Follow-up:

I. In hospital complications of studied groups:

Eighty seven (96.67%) of patients passed without any complications. Only 3 (3.33%) of patients presented by in hospital acute ST elevation myocardial infarction (STEMI) detected by acute onset of chest pain, elevated cardiac enzymes and new ST-T wave changes in the ECG, 2 (3.03%) of patients in group A and 1 (4.17%) of them in group B, which presented no significant differences. But, no in hospital mortality or arrhythmias and none of them needed urgent revascularization (Table 4).

Table (4): In hospital complications.

Parameter	Group A	Group B	P-value
	n=66	n=24	
No Complications	64(96.97%)	23(95.85%)	>0.05
Post-Catheter Acute STEMI	2(3.03%)	1(4.17%)	>0.05
In hospital Mortality	0 (0%)	0 (0%)	0
Urgent revascularisation	0 (0%)	0 (0%)	0
Post-catheter arrhythmias	0 (0%)	0 (0%)	0

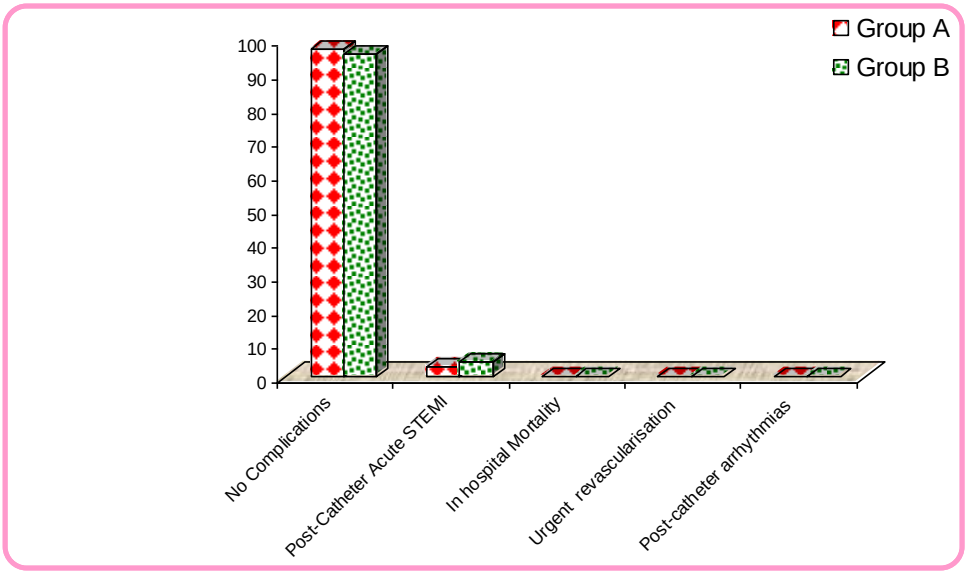


Fig. (7): In hospital complications.

II. Adverse clinical events of follow-up of studied groups:

Patients were followed by regular visits and telephone calls for occurrence of rest angina, MI, hospitalization for acute coronary syndrome (ACS), coronary revascularization and mortality with mean duration of 6.83 ± 1.04 months.

Patients with adverse end points were asked to come and their medical records were received, 72 (80%) of patients passed without complications, 2 (8.3%) of patients from group B developed STEMI within 6 months but none of group A, which presented non significant differences.

Sixteen (17.78%) of patients needed coronaries revascularization, 6 (9.09%) of patients in group A, and 10 (41.67%) of them in group B which presented significant difference. Neither mortality nor cardiac arrhythmias occurred (Table 5).

Table (5): Late follow up results.

Parameter	Group A	Group B	P-value
	n=66	n=24	
No Complication	60(90%)	12(50%)	<0.05*
STEMI	0 (0%)	2(8.33%)	>0.05
Need for revascularisation	6(9.09%)	10(41.67%)	<0.05*
Mortality	0 (0%)	0 (0%)	0
Arrhythmias	0(0%)	0 (0%)	0

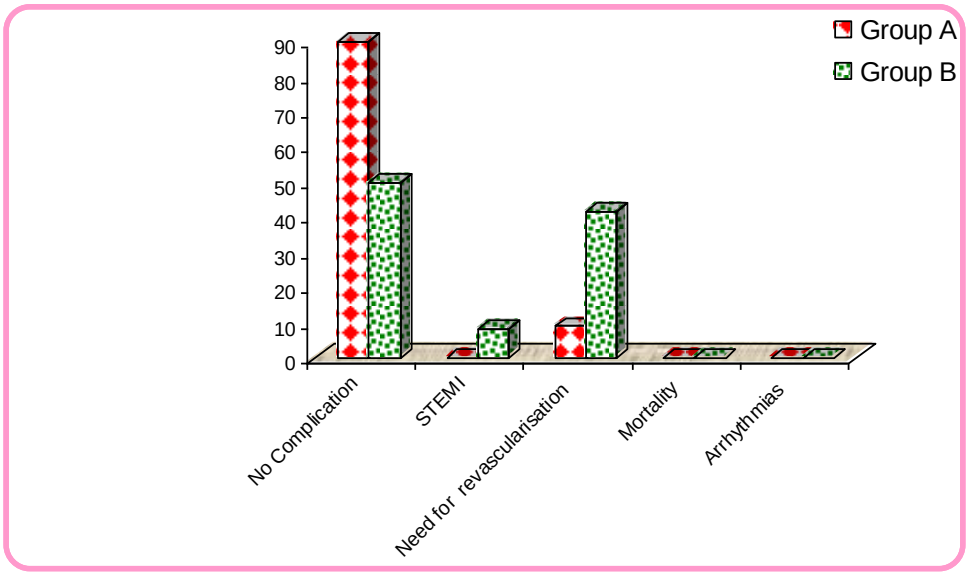


Fig. (8): Follow-up complications.

Predictors of cardiac Tn-I elevation and cardiac Tn-T elevation after coronary intervention:

(a) Abnormal markers distribution:

In the current study, cardiac troponins were measured at base line, 12 hrs and 24 hrs after the intervention. 69 (76.67%) of patients showed no elevation of cardiac Tn-I (i.e. <2 ng/mL). while, 21 (23.33%) of patients showed significant elevation of serum level of cardiac Tn-I(i.e. >2 ng/mL), 15 (24.24%) of patients in group A and 6 (20.83%) of them in group B.

Seventy two (80%) of patients showed no elevation of cardiac Tn-T (i.e. <0.01 ng/mL). while, 18 (20%) of patients showed significant elevation of cardiac Tn-T (i.e.>0.1 ng/mL), where 14 (21.21%) of patients in group A and 4 (16.67%) of them in group B.

The frequencies of abnormal cardiac Tn-I and cardiac Tn-T in group A were not significantly higher than group B (Table 6).

Table (6): Distribution of cardiac troponins.

Cardiac Troponins	Group A	Group B	Total	P-value
	n=66	n=24	n=90	
No elevation	37(56.06%)	14(58.33%)	51(56.67%)	>0.05
elevated Tn-I	16(24.24%)	5(20.83%)	21(23.33%)	>0.05
elevated Tn-T	14(21.21%)	4(16.76%)	18(20%)	>0.05

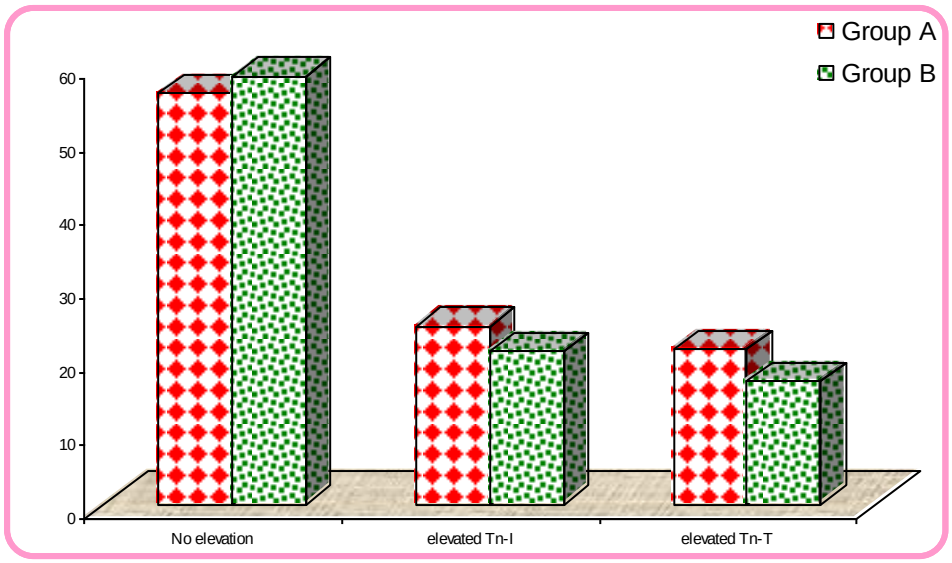


Fig. (9): Distribution of cardiac troponins.

(b) Baseline clinical parameters of both the studied groups in relation to Tn-I:

Clinical parameters of both groups were studied independently in correlation with cardiac Tn-I, there was no significant differences in age of patients (i.e. 49±5.31 versus 52.71±7.73 yrs), 63 (92.31%) versus 18 (85.71) of patients were males, and 6(8.69%) versus 3(14.29%) of them were females.

Regarding risk factors, diabetic, dyslipidemic and smoker patients cleared significant differences i.e. 9 (13.3%) versus 9 (42.86%), 33 (47.83%) versus 18(85.72%), and 27 (39.13%) versus 15 (71.43%) of patients respectively.

Hypertensive and obese patients showed no significant differences between the studied groups i.e. 27 (39.13%) versus 9 (42.85%) and 18 (26.09) versus 3 (14.29%) of patients respectively (Table 7).

Table (7): Base-line clinical parameters of the studied groups.

Character	Troponin I -ve	Troponin I +ve	P-value
	n = 69	n=21	
▪ Age (mean ± SD) yr	49 ± 5.31	52.71±7.73	>0.05
▪ Sex			
Males	63 (92.31%)	18 (85.71%)	>0.05
Females	6 (8.69%)	3 (14.29%)	>0.05
▪ Risk factors			
DM (number, %)	9 (13.13%)	9 (42.86%)	<0.05*
HTN (number, %)	27 (39.13%)	9 (42.86%)	>0.05
Dyslipidemia (number, %)	33 (47.83%)	18 (85.72%)	<0.05*
Smoking (number, %)	27 (39.13%)	15 (71.43%)	<0.05*
Obesity (number, %)	18 (26.09%)	3 (14.29%)	>0.05

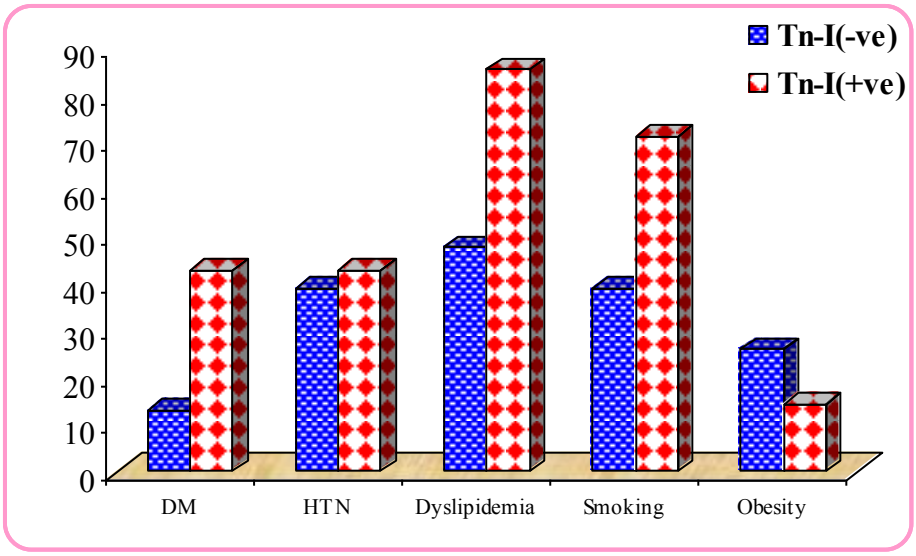


Fig. (10): Significance of risk factors of the studied groups.

(c) Coronary angiographic parameters of both the studied groups in relation to Tn-I and lesion characteristics:

Regarding the type of lesion, type B lesion showed significant differences, but type A and C lesions showed no significant differences (Table 8).

Table (8): Coronary angiographic parameters of the studied groups in relation to Tn-I and lesion characteristics.

Parameters		Troponin I -ve n=69	Tropnin I +ve n=21	P-value
Type of lesion (Number, %)	A	39(56.52%)	9(42.66%)	>0.05
	B	21(30.43%)	12(57.14%)	<0.05*
	C	9(13.04%)	0 (0%)	>0.05

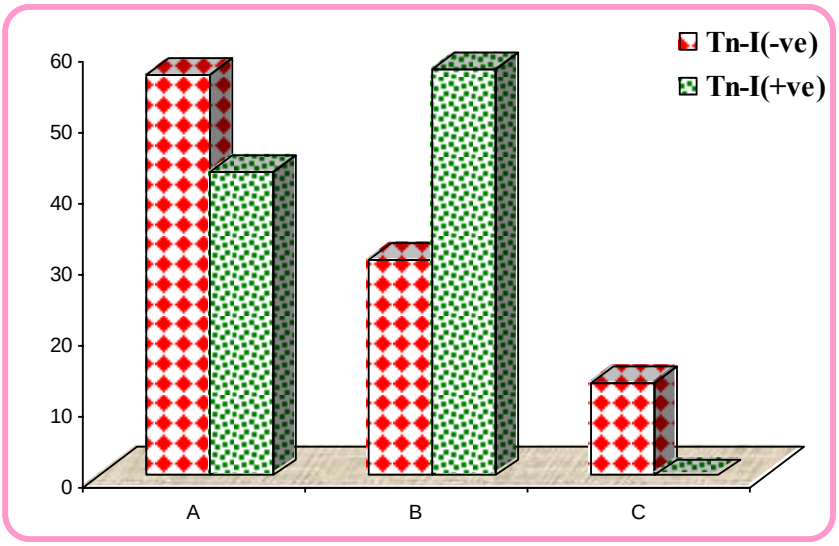


Fig. (11): Coronary angiographic parameters of the studied groups in relation to Tn-I and lesion characteristics.

(d) The relation of interventional characteristics of both the studied groups to cardiac Tn-I:

In the study, patients with prolonged total time of balloon inflations or increased maximal pressure of balloon inflations were associated with post intervention Tn-I elevation which cleared significant differences (Table 9).

Table (9): The relation of interventional characteristics of both the studied groups to cardiac Tn-I.

Parameter	Troponin I -ve n=69	Tropnin I +ve n=21	P-value
Total number of inflations	2.7±1.4	3.4±1.9	>0.05
Total time of inflations (sec.)	164±101	248±103	<0.05*
Longest Single inflation (sec.)	63±6	69±9	<0.05*
Maximal pressure of inflation (atm.)	18±12.9	21±12	<0.05*
Balloon diameter(mm)	2.25±0.45	2.7±0.25	>0.05
Occurrence of side branch occlusion	5(7.25%)	13(61.9%)	<0.05*

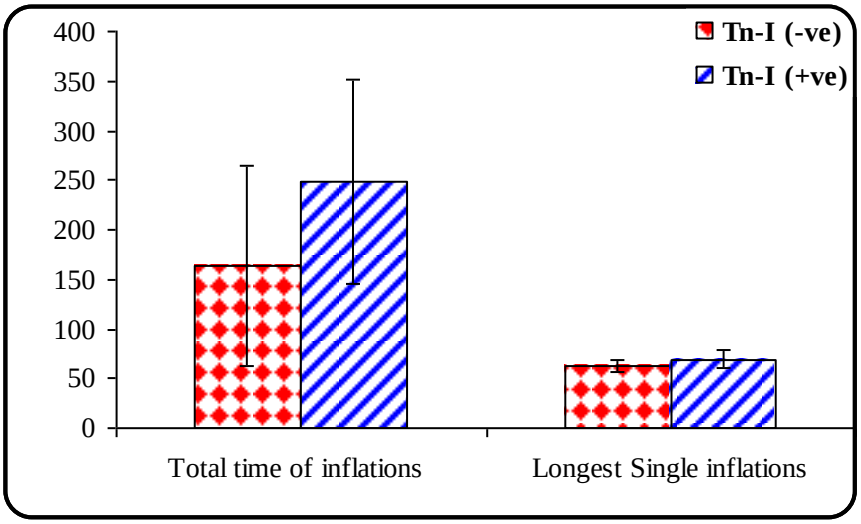


Fig. (12): The relation of interventional characteristics of both the studied groups to cardiac Tn-I.

Where, number of balloon inflations showed non significant correlation with cardiac Tn-I, and also balloon diameter was not associated with significant difference.

Occurrence of side branch occlusion showed significant difference in patients with elevated Tn-I (Table 9).

(e) Clinical presentations of both groups before the coronary angioplasty in relation to cardiac Tn-I:

Regarding clinical presentations of both groups before the coronary angioplasty, there were no significant differences of electrocardiographic and echocardiographic parameters of both groups before the intervention in relation to cardiac Tn-I (Table 10).

Table (10): Clinical presentations of both groups before the coronary angioplasty in relation to cardiac Tn-I.

Parameters	Troponin I -ve	Tropnin I +ve	P.value
	n=69	n=21	
ECG			
- ST-T wave changes	48 (69.57%)	6 (28.57%)	>0.05
- Pathological Q wave	12 (17.39%)	6 (28.47%)	>0.05
- Normal	9 (13.04%)	3 (14.26%)	>0.05
Echocardiography			
- FS %	27.47 ± 4.84	27.71 ± 5.82	>0.05
- EF %	54.73 ± 7.49	54.14 ± 9.47	>0.05
- >55 %	66 (95.65%)	18 (85.72%)	>0.05
<55 %	3 (4.35%)	3 (14.29%)	>0.05
- EDD mm	52.64 ± 2.49	56.24 ± 3.70	>0.05
- ESD mm	33.1 ± 1.98	33.37 ± 2.49	>0.05

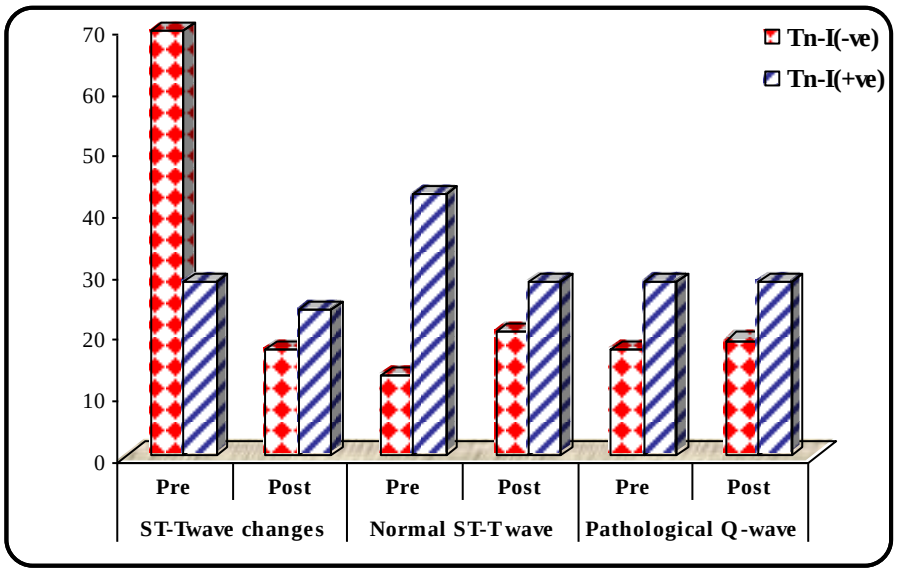


Fig. (13): Significance of ECG parameters of the studied groups in relation to Tn-I elevation.

(f) Clinical presentations of both groups after the coronary angioplasty in relation to cardiac Tn-I:

Follow-up showed no significant differences in patients with new ST-elevation myocardial infarction or new ST segment depression as indicator of anginal attacks and elevated Tn-I.

Echocardiography showed significant differences in left ventricular function (EF %) and dimensions i.e. end diastolic dimensions and end systolic dimensions regarding elevated cardiac Tn-I.

Table (11): Clinical presentations of both groups after the coronary angioplasty.

Parameters	Troponin I -ve	Tropnin I +ve	P.value
	n=69	n=21	
Post catheter ECG (number, %)			
- New ST-segment elevation	3 (4.35%)	2 (9.52%)	>0.05
- New ST-segment depression or T-wave abnormality	9 (13.04%)	3 (14.29%)	>0.05
- Normalized St segment	13 (18.84%)	6 (28.57%)	>0.05
- Pathological Q wave	14 (20.29%)	8 (38.1%)	>0.05
- Normal	30 (43.47%)	2 (9.52%)	>0.05
Post-catheter ECHO			
- FS %	29.03 ± 5.54	21.8 ± 5.71	<0.05*
- EF %	57.16 ± 7.51	45.55 ± 8.36	<0.05*
>55%	67 (97.11%)	5 (23.81%)	<0.05*
<55 %	2 (2.99%)	16 (76.19%)	<0.05*
- EDD (mm)	55.01 ± 2.13	56.27 ± 4.0	<0.05*
- ESD (mm)	33.6 ± 2.16	33.3 ± 3.2	<0.05*

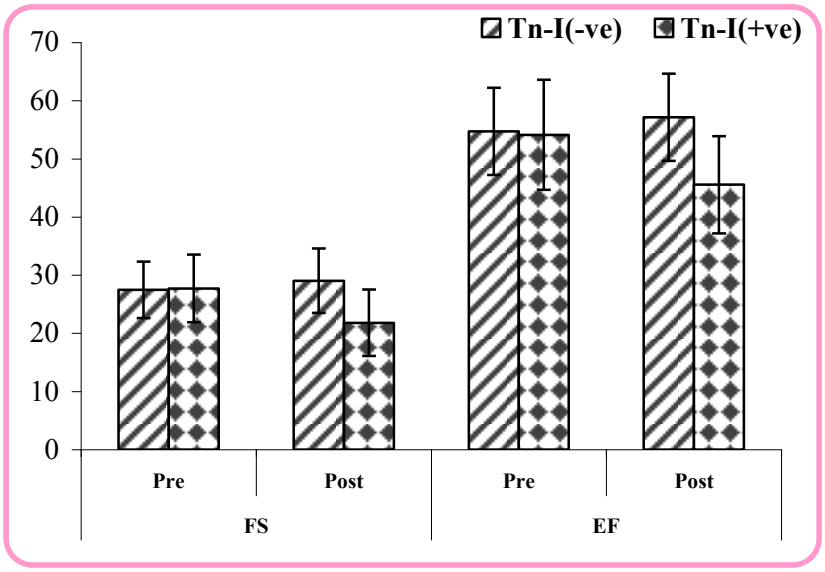


Fig. (14): Significance of ECHO parameters of the studied groups in relation to Tn-I elevation.

(g) Quantitative angiographic analysis (QCA) of the lesion:

Study of the interventional variables i.e. minimal luminal dimensions (MLD) and distance of stenosis (DS %) showed no significant differences in patients with elevated Tn-I before the intervention, but cleared significant differences after the intervention (Table 12).

Table (12): Interventional variables of the studied groups.

Parameters	Troponin I -ve	Tropnin I +ve	P.value
	n=69	n=21	
Pre-catheter MLD (mm)	3.99 ± 2.21	4.77 ±2.27	>0.05
DS %	8.45 ± 4.02	8.33 ± 4.00	>0.05
Post-catheter MLD (mm)	7.72 ± 2.01	7.41 ± 2.16	<0.05*
DS %	13.81 ± 2.22	11.62 ± 3.02	<0.05*

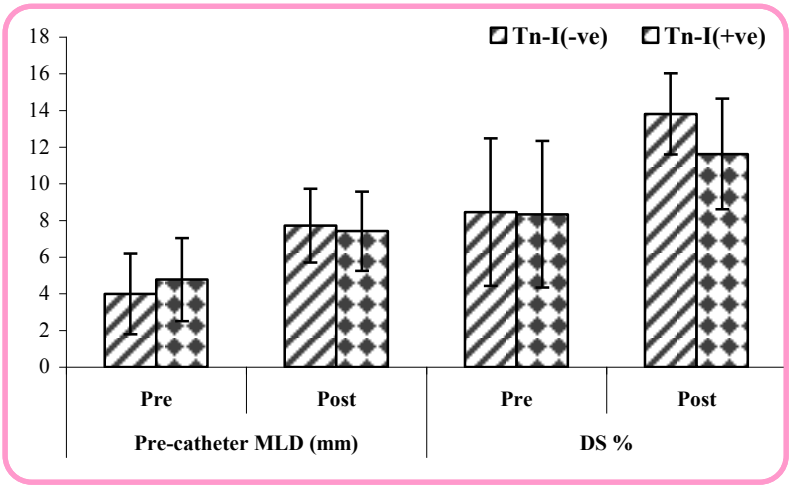


Fig. (15): Interventional variables of the studied groups.

(h) Early adverse clinical events of the studied groups in relation to Tn-I:

In the present study, post intervention early occurrence of acute myocardial infarction (STEMI) showed no significant differences in patients with elevated Tn-I.

There was significant need to repeat coronary angiography in patients with post intervention elevated Tn-I but, there was no mortality (Table 13).

Table (13): Early adverse clinical events of the studied groups in relation to Tn-I.

Parameters	Troponin I -ve	Tropnin I +ve	P-value
	n=69	n=21	
STEMI	1(1.45%)	1(4.76%)	>0.05
Need for revascularisation	0 (0%)	2(9.52%)	<0.05*
Mortality	0 (0%)	0 (0%)	0

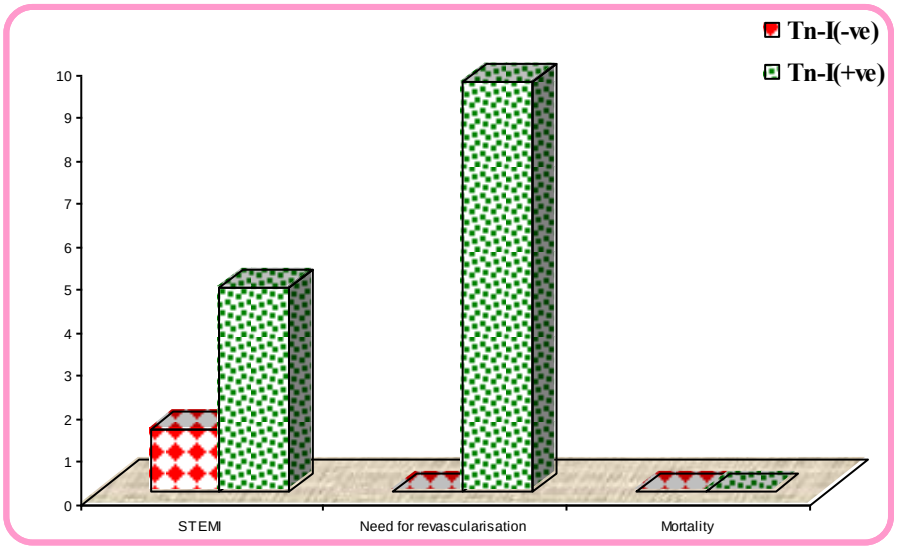


Fig. (16): Early adverse clinical events of the studied groups in relation to Tn-I.

(i) Adverse clinical events at follow-up of the studied groups in relation to Tn-I:

During six months follow up, there was no significance of occurrence of STEMI in patients with elevated cardiac Tn-I.

There was also significant need to repeat the coronary intervention. No mortality occurred (Table 14).

Table (14): Adverse clinical events at follow-up of the studied groups in relation to Tn-I.

Parameters	Troponin I -ve n=69	Troponin I +ve n=21	P-value
STEMI	1(1.45%)	1(4.76%)	>0.05
Need for revascularisation	6(9.8%)	8(38.09%)	<0.05*
Mortality	0 (0%)	0 (0%)	0

Sens.	Spec.	PPV	NPV	Accuracy
38.095	91.304	57.143	82.895	78.889

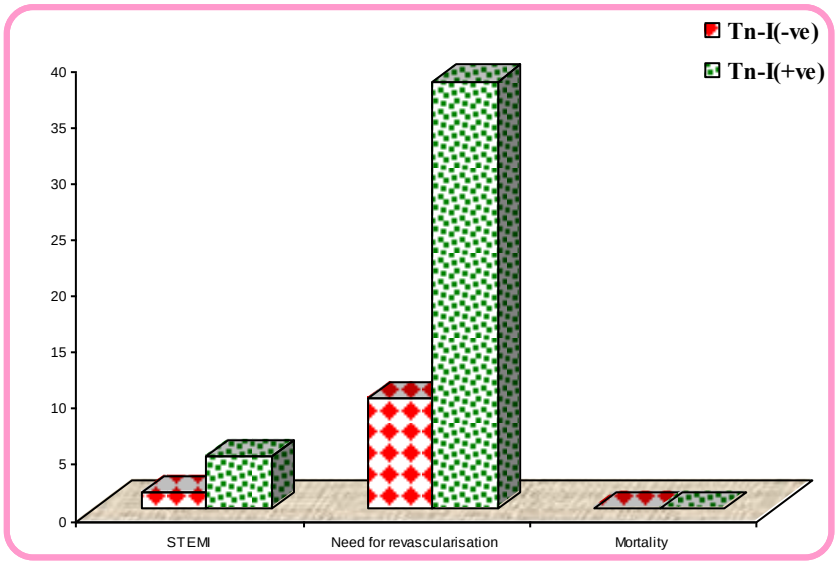


Fig. (17): Adverse clinical events at follow-up of the studied groups in relation to Tn-I.

Case (39):

P.H.: Male patient, 57 years old,married,has 3 children and has history of DM, and elevated serum lipids.

F.H.: +ve family history of DM and CAD.

E|O: Bl. Pr., 120|80, Pulse 80 bpm, regular

Heart, S1+S2

Chest, normal vesicular breath with clear back

Abdomen, lax with no organomegally

Normal neck veins and lower limbs

ECG: Regular at 80bpm, isoelectric ST-segment, flattened T-wave in V1-V4,

ECHO: FS% 20%, EF% 44%, EDD 56.1mm, ESD 34.1mm anteroseptal hypokinesia

Angiography: Single proximal LAD lesion, 90%, concentric, type A

Angioplasty: Successful balloon dilatation & stent implantation of the lesion with no dissections or side branch occlusion

Follow up:

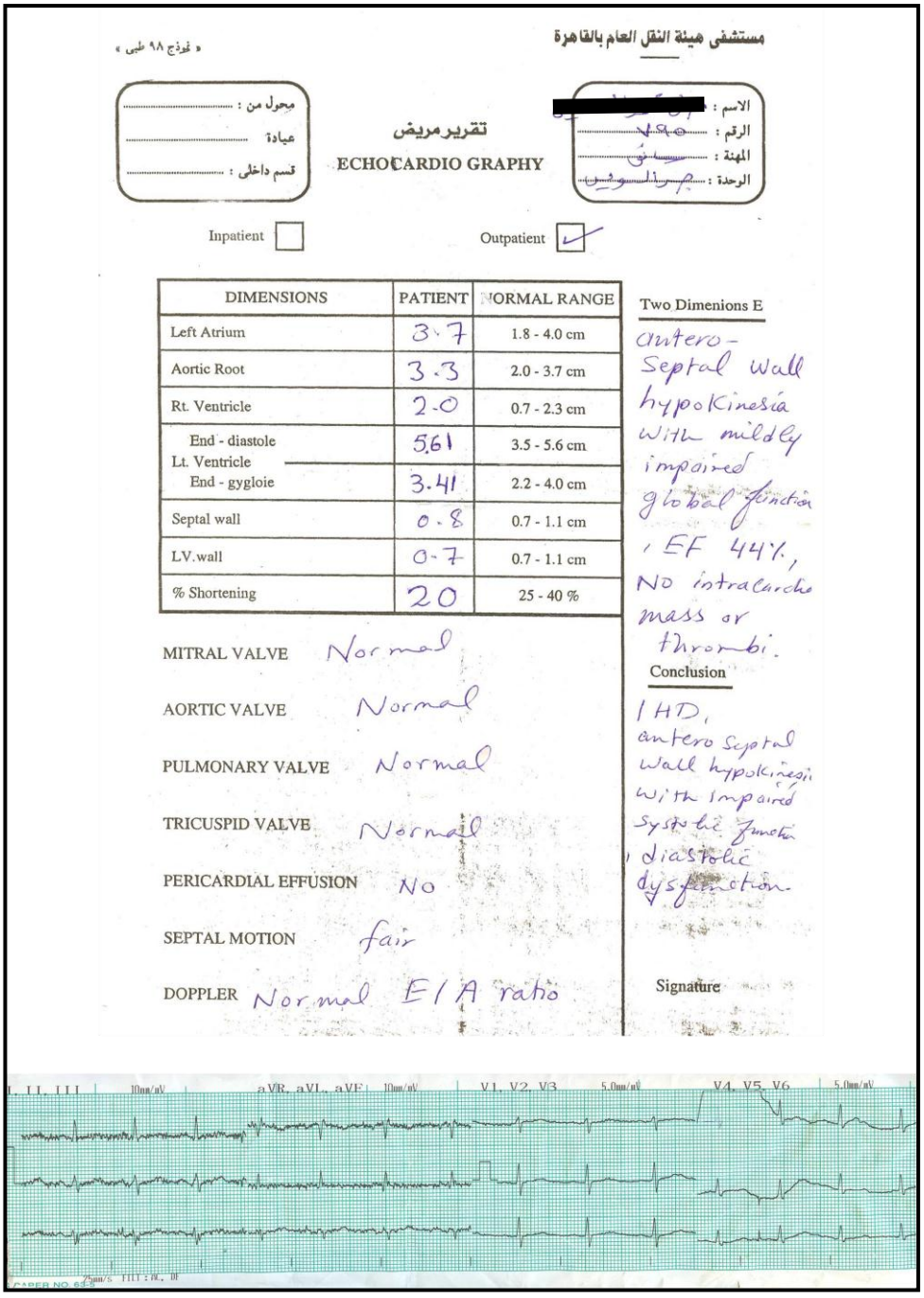
ECG: Normal trace

ECHO: FS% 22%, EF% 50%, EDD 55.5mm, ESD 33.5mm

Troponins: Tn-I at baseline 1.33, at 12hrs 2.0, at 24hrs 2.31 ng|ml

Tn-T at baseline 0.01, at 12hrs 0.05, at 24hrs 0.11 ng|ml

No follow up adverse cardiac events.



مستشفى هيئة النقل العام بالقاهرة

« نموذج ٩٨ طبى »

محول من : .....
عيادة .....
قسم داخلى : .....

تقرير مريض

ECHOCARDIO GRAPHY

الاسم : [redacted]
الرقم : .....
المهنة : .....
الوحدة : .....

Inpatient ☐ Outpatient ☑

DIMENSIONS	PATIENT	NORMAL RANGE
Left Atrium	3.7	1.8 - 4.0 cm
Aortic Root	3.3	2.0 - 3.7 cm
Rt. Ventricle	2.0	0.7 - 2.3 cm
Lt. Ventricle End - diastole	5.61	3.5 - 5.6 cm
Lt. Ventricle End - gygloie	3.41	2.2 - 4.0 cm
Septal wall	0.8	0.7 - 1.1 cm
LV.wall	0.7	0.7 - 1.1 cm
% Shortening	20	25 - 40 %

MITRAL VALVE Normal

AORTIC VALVE Normal

PULMONARY VALVE Normal

TRICUSPID VALVE Normal

PERICARDIAL EFFUSION No

SEPTAL MOTION fair

DOPPLER Normal E/A ratio

Two Dimenions E

antero-Septal Wall hypokinesia with mildly impaired global function, EF 44%, No intracardiac mass or thrombi.

Conclusion

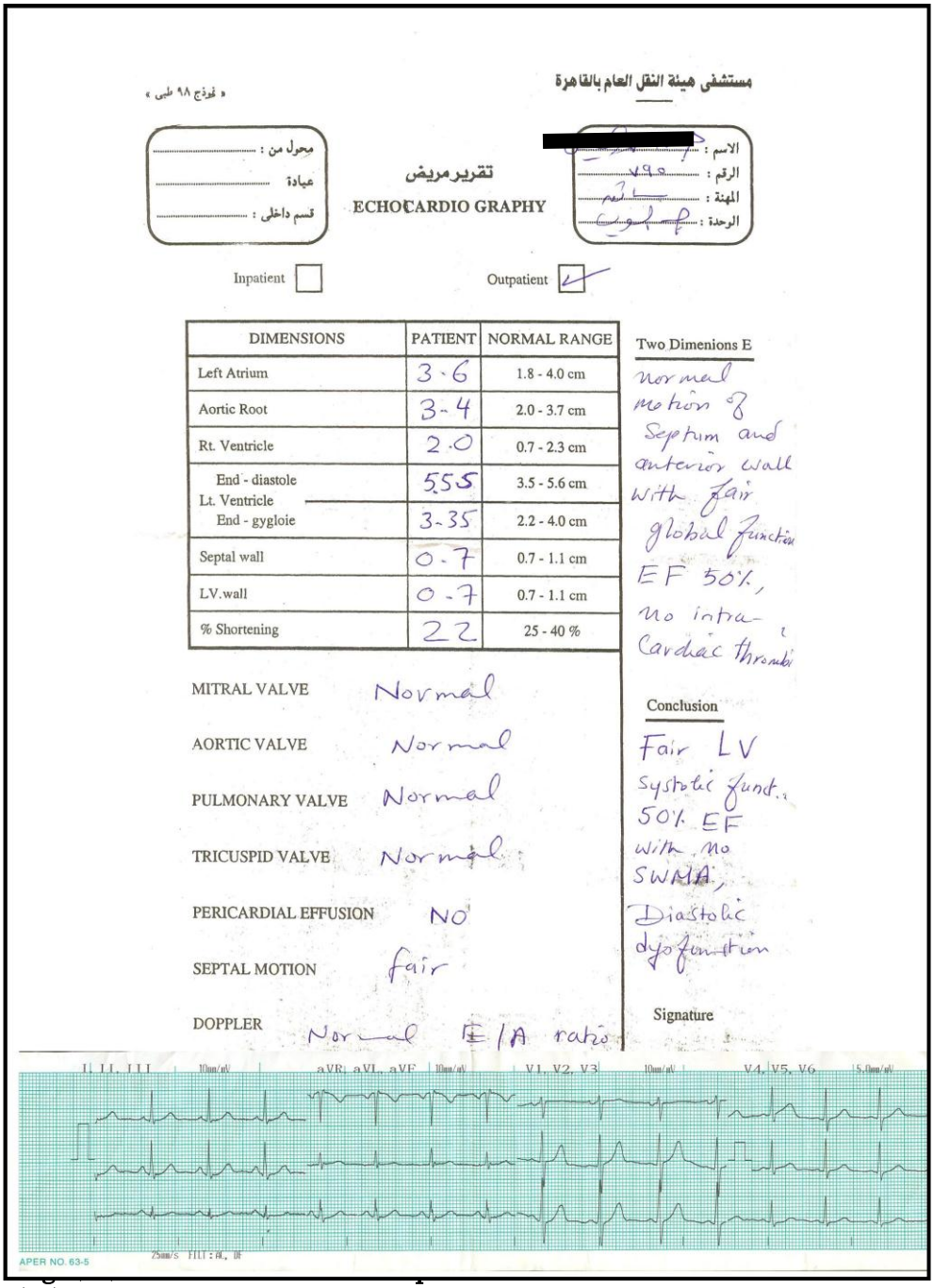
IHD, antero Septal Wall hypokinesia with impaired systolic function & diastolic dysfunction.

Signature

I, II, III 10mm/mV aVR, aVL, aVF 10mm/mV V1, V2, V3 5.0mm/mV V4, V5, V6 5.0mm/mV

CASE NO 63-3

Fig. (18): ECG and ECHO interpretations before the intervention of case (39).



« نموذج ٩٨ طبى »

مستشفى هيئة النقل العام بالقاهرة

محول من : .....
عيادة .....
قسم داخلى : .....

تقرير مريض
ECHOCARDIO GRAPHY

الاسم : [redacted]
الرقم : ٧٩٥
المهنة : ...
الوحدة : ...

Inpatient ☐ Outpatient ☑

DIMENSIONS	PATIENT	NORMAL RANGE
Left Atrium	3.6	1.8 - 4.0 cm
Aortic Root	3.4	2.0 - 3.7 cm
Rt. Ventricle	2.0	0.7 - 2.3 cm
Lt. Ventricle End - diastole	5.5	3.5 - 5.6 cm
Lt. Ventricle End - gygloie	3.35	2.2 - 4.0 cm
Septal wall	0.7	0.7 - 1.1 cm
LV.wall	0.7	0.7 - 1.1 cm
% Shortening	22	25 - 40 %

MITRAL VALVE Normal
AORTIC VALVE Normal
PULMONARY VALVE Normal
TRICUSPID VALVE Normal
PERICARDIAL EFFUSION NO
SEPTAL MOTION fair
DOPPLER Normal E/A ratio

Two Dimenions E
Normal motion of Septum and anterior wall with fair global function EF 50%, no intra-cardiac thrombi

Conclusion
Fair LV systolic funct., 50% EF with no SWMA, Diastolic dysfunction

Signature

(39).

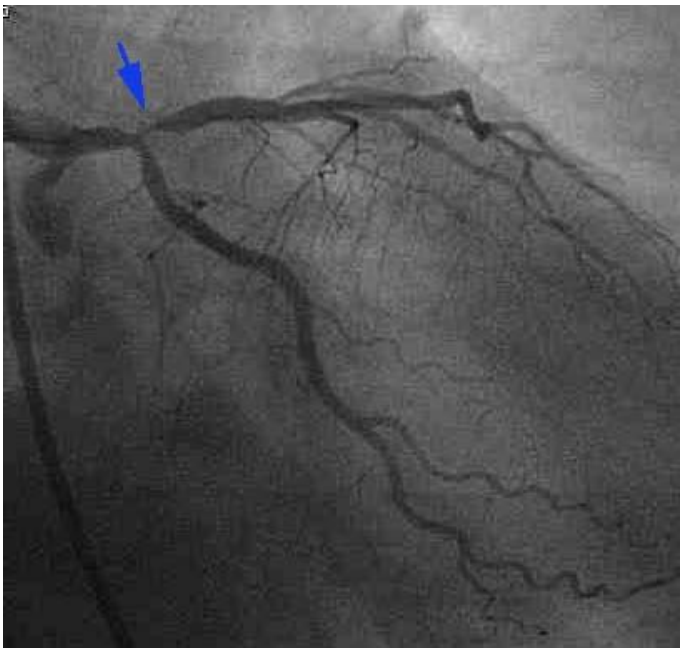


Fig. (20): Anterior view of left anterior descending coronary artery showing tight proximal stenosis of case 39.

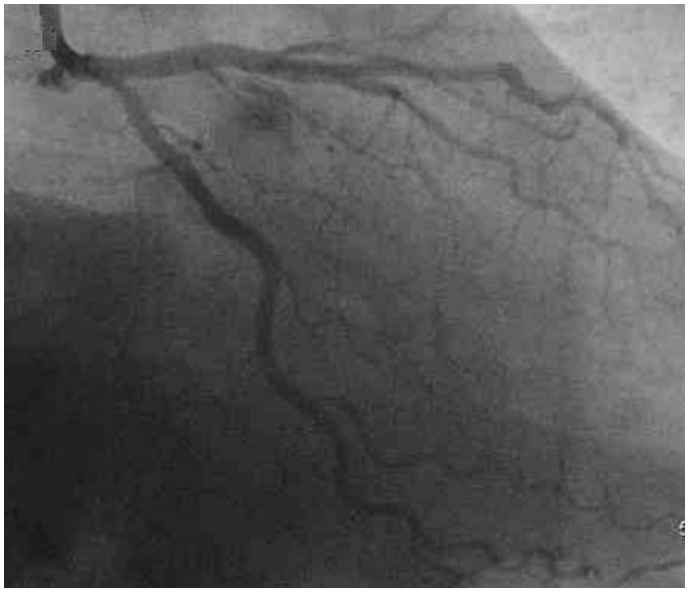


Fig. (21): Anterior view showing stent implantation to stenotic proximal LAD lesion of the same case.

Discussion

During the past three decades, percutaneous coronary intervention has become one of the cardinal treatment strategies for stenotic coronary artery diseases. Technical advances including the introduction of new devices such as stents have expanded the interventional capabilities of balloon angioplasty.

Despite these advances, the incidences of post-procedural cardiac markers elevation haven't substantially decreased since the first serial assessment 20 years ago. As of now, elevation of these post procedural cardiac markers is considered to represent periprocedural myocardial injury (PMI) with worse outcome potential.

Owing to the improvement in interventional techniques and expertise as well as, the introduction of new devices, such as stents, the incidence of major periprocedural ischemic complications such as acute myocardial infarction (AMI), CABG or death are reduced initially from 9% to currently less than 2% *(Tongi et al., 2004).*

In clinical practice, the demonstrated cardiac markers elevation has been used as an important criterion for the diagnosis of myocardial necrosis. This concept stems from the assumption that once the intracellular enzymes start leaking

from the myocardial cells, cellular injury has revealed a stage of irreversibility *(Geft et al., 1982).*

However, the incidence of post procedural cardiac marker elevation has not substantially declined since its first serial assessment by *Oh et al. (1985).*

In analogy to acute myocardial infarction, elevated cardiac markers are considered to reflect periprocedural myocardial injury or infarction *(Callif et al., 1998).*

The term "myocardial injury" has been used to describe any kind of impairment of regular myocardial homeostasis, which can lead to reversible or irreversible alteration in myocardial function and structure. A number of different etiologies including mechanical, infectious, metabolic or toxic causes *(Callif et al., 1998).*

In the setting of PCI, myocardial injury is mainly metabolic in origin relating to ischemia. The fact that currently applied diagnostic methods doesn't reflect all myocardial alternations taking place in quantity or quality *(Katoh et al., 2000).*

For example, the ice berg phenomenon demonstrated the peripheral venous cardiac Tn-T concentration in their discrepancy to coronary sinus cardiac Tn-T concentration following percutaneous transluminal coronary angioplasty

(PTCA). Furthermore, experimental studies indicated that reversible myocardial injury might yield positive cardiac markers results *(Feng et al., 1998).*

Johansen et al. (1998) and *Rimppis et al. (2000)* demonstrated that the majority of cardiac Tn-T elevations within 24 hrs after PCI persist up to 96 hrs indicating ongoing release of cardiac Tn-T from the contractile apparatus and hence irreversible myocardial injury.

In the present study, 90 patients were known to have significant proximal LAD lesion diagnosed by previous coronary angiography. All patients were prepared for balloon dilatation and stents were implanted in 66(73.33%) of patients. A comparative study of the PTCA and the PTCA with stent groups demonstrated non significant differences in age, sex or risk factors for coronary artery disease.

This was in agreement with *Saadeddin et al. (2002)* who studied 98 patients, 75 males, and 23 females with mean age of 53$\pm$11 years, P-value >0.05.

In the studied groups, pre- and post angiographic parameters including lesion length were in consistent with *Timur et al. (2002)* who studied 60 patients prepared for direct versus conventional stenting, lesion lengths were non significantly different in the studied groups i.e. 11.1$\pm$39 versus 11.3$\pm$3.4 mm, P-value >0.05.

The current study demonstrated that the coronary interventions were fulfilled both the clinical and angiographic criteria of success including proper pre-intervention preparation, balloon inflation, stent implantation, and post-intervention ICU admission for 24 hours. Records showed non significant complications occurred in the studied groups including acute STEMI, early arrhythmias, urgent revascularization or in-hospital mortality. Table (4)&Fig. (7).

These results disagreed with ***Prasad et al. (2008)*** who studied 2352 patients referred to elective PCI, patients who showed no baseline elevation of cardiac Tn-T had significant rate of acute MI or death (4.7%), P-value <0.05 may be due to large sample size and criteria of selected patients.

During 6 months follow-up, the PTCA group cleared significant need to repeat the coronary angiography especially in patients with elevated cardiac Tn-I. But, other adverse cardiac events as recurrent MI or death cleared non significant differences of the studied groups. Table (5) & Fig.(8).

Predictors of cardiac Tn-I and Tn-T elevation after the coronary intervention:

The frequencies of cardiac Tn-I and Tn-T elevation in the PTCA + Stent group were not significantly higher than the PTCA only group, P-value >0.05. Table (6) & Fig. (9).

These results were comparable to those of *Saadeddin et al. (2001)* who cleared that cardiac Tn-I and Tn-T elevation were non significant between the studied groups i.e. 21.1% versus 11.1% and 29.6% versus 18.5% respectively, P-value >0.05.

By study of clinical parameters, age, sex, elevated blood pressure and obesity showed non significant correlations with elevated cardiac Tn-I; while, diabetes mellitus, smoking, and elevated serum lipids as independent predictors were associated with significant correlation with elevated Tn-I. Table (7) & Fig. (10).

This was concordant with *Izgi et al. (2006) and Okmen et al. (2006)* results in their studies which concluded that there was no correlations between age or gender and Tn-I elevation, P-value >0.05.

Results were in correlation with the study of *Saadeddin et al. (2001)* who cleared no significance of age and gender (male/female) on Tn-I elevation in a sample of 98 patients i.e. 55$\pm$11 versus 56$\pm$13, 89% versus 64.29% and 20% versus 35.71% respectively, P-value 0.05.

Also, *Jean-Pierre et al. (1999)* studied 105 patients prepared for PTCA of single or mutlivessel disease in stable and unstable angina pectoris which showed non significant correlation of age and sex to elevated cardiac Tn-I, i.e. 60$\pm$11 versus 63$\pm$11, 73.39% versus 78.26% and 25.6% versus 21.74% respectively, P-value >0.05.

A study by *Shmuel et al. (2001)* of 132 patients presented by acute coronary syndrome showed borderline significance of age in elderly patients with elevated Tn-I, i.e. 64±12 versus 68±13, P-value =0.05. And DM was independent predictor of elevated cardiac Tn-I especially in older patients i.e. 3% versus 30%, P-value <0.05.

In Sirofiban versus aspirin to yield maximum protection from ischemic heart events post acute coronary syndromes trial (SYMPHONY) *Warren et al. (2002)* randomized 9.233 patients presented by acute coronary syndromes to receive Aspirine 80 mg or Sirofiban twice daily for 90 days and elective PCI. The study cleared that DM has non significant correlation to elevated Troponin-I, i.e. 14.8% versus 20.3%, P-value >0.05 these statistical differences may be due to large sample size of this study.

The study results were in agreement with those of *Augardro et al. (2006)* who studied 552 patients and showed that patients on chronic statin therapy had lower incidence of post- PCI cardiac Tn-I elevation versus patients who were not on statins i.e. 29% versus 48%, P-value <0.001).

In the last years, increasing evidence supported many other effects of statins beside lipid lowering effects, including improvement of endothelial functions, plaque stability, reduction in oxidative stress, inflammation, platelets activation; and thrombosis. All these effects might not be related to the reduction of cholesterol levels but they are

likely to drive from the pleiotropic effects of statins *(Bickel et al., 2002).*

In the present study, regarding the clinical presentations of both the studied groups in relation to cardiac Tn-I elevation, the ECG analysis showed no significant ST-T waves changes after the intervention, and ECHO study showed significantly decreased ejection fraction (EF%) in patients with increased cardiac Tn-I. Table (8) & Fig. (11)

Regarding angiographic parameters, patients who underwent prolonged total time of balloon inflations, prolonged total time of single inflation, as well as increased maximal pressure of balloon inflations cleared significant correlation with elevated Tn-I. Side branch occlusion showed significant relation to it that may be due to plaque dissection and cholesterol debris liberation after balloon inflation. Table (9) & Fig. (12).

These results were in agreement with *Saadeddin et al. (2001)* who recorded that post intervention abnormal cardiac Tn-I and Tn-T values were significantly related to the total time of balloon inflation (sec.) and maximal pressure of the inflations (atm.) i.e. 170$\pm$105, versus 223$\pm$128 sec, and 12.0$\pm$27 versus 12.9$\pm$23 atm. Respectively, P-value <0.05. Side branch occlusion was noticed in 36% of Tn-I +ve patients and 6% of Tn-I –ve patients which was highly significant, P-value <0.01.

Results of a study by *Timur et al. (2002)* were different, who studied direct stenting against conventional stenting in 60 patents were known to be in stable or unstable angina pectoris, total time of balloon inflation and inflation maximal pressure cleared non significant relation to elevated Tn-I, i.e. 43.1±24 versus 54.4±23.9, and 14±1.2 versus 13.4±2 respectively, may be due to small sample size, or selected patients criteria.

But, the results of the current study were concordant with *Izgi et al. (2006)* in a study that included 100 patients, the troponin I +ve group including 27 patients showed that there was a significant correlations between psotprocedural troponin I elevation and the total time of balloon inflations i.e. 169±1-7 versus 209±104, P=0.001.

Regarding the study by *Jean-Pierre et al. (1999)*. By multivariate logistic registration, the most significant predictor of post-procedure cardiac Tn-I elevation was the longest inflation time of ≥90 sec. (P-value = 0.001), followed by B lesion morphology according to American Heart Association and American Collage of Cardiology AHA/ACC (P-value = 0.013). Other important predictors include age ≥60 years (P-value = 0.032) and unstable angina (P-value=0.041).

Some minor clinical complications such as side branch compromise, distal micro-embolization, dissections or transient vessel closure have been found to be associated with an increase in enzymes after successful PTCA, consistent with the hypothesis that enzyme elevation may be associated

with sustained decreases in perfusion to small myocardial territories.

In the current study, early after hospital discharge one patient with cardiac Tn-I +ve developed STEMI and one patient with cardiac Tn-I –ve which were non significant, two patients with Tn-I +ve needed revascularization after 1 month of the intervention but non of Tn-I –ve patients needed early revascularization which was significant, P-value <0.05. No mortality occurred. Table (13) & Fig. (16).

Six months follow up demonstrated that one patient with post procedural Tn-I +ve and one patients with Tn-I –ve developed acute STEMI which were statistically non significant, 8 patients with Tn-I +ve needed revascularization (38.09%) and 6 patients with Tn-I–ve needed revascularization (9.8%) which demonstrated statistical significance, no follow up mortality occurred. Table (14) & Fig. (17).

The study results were in disagreement with those of *Schmuel et al. (2001)*, who studied 132 patients presented by acute coronary syndrome and have single or multivessels diseases and demonstrated significant relation between death and elevated Tn-I but STEMI and need for revascularization didn't i.e. 3.7% versus 24%, 1.2% versus 2% and 12% versus 14% respectively.

In his study, patients with Tn-I re-elevation had higher rate of in hospital mortality and was secondary to cardiac

causes in 4 patients (cardiogenic shock in 3 patients and sudden cardiac death in one patient), and those patients had history CABG, NSTEMI, low EF%, or multivessels disease.

Finally, we conclude that cardiac Tn-I is an extremely sensitive marker that detect even reversible myocardial injury caused by procedure induced ischemia, or very minor myocardial necrosis, and this in agreement with *Cavillani et al. (2005).*

Study Limitations

- This study was non randomized, performed on small sample size of patients (ninety patients).
- Single vessel selection (LAD) with proximal De Novo lesion. Where, multivessel lesions, patients with acute coronary syndromes (ACS), recent STEMI, history of PCI or CABG were excluded.
- The study may not be applicable on drug-eluting stents as this type of stents was not studied as separate variable.

All these may have limited the statistical power to detect a significant difference in enzyme elevation between the studied groups and the ability to detect the predictors of troponins elevation.

However, these data provided a framework for larger prospective studies in patients undergoing PTCA and stent implantation. Randomized studies with larger patient populations should be conducted to compare the two different approaches.

Conclusion

Based on the results of the current study, it could be concluded that:

- The most important predictors of post PCI cardiac troponin I elevation were occurrence of coronary dissections after the PTCA which were more significant with increasing time of balloon inflation (sec.) or increasing maximal pressure of inflation (atm.).

- Patients underwent PTCA only were more brone for distal microembolization and side branch occlusion than patients with PTCA and stent implantation, thus increased the incidence of follow up need for revascularization.

- Occurrence of side branch occlusion was associated with significant elevation of cardiac markers without identifiable angiographic adverse cardiac events such as chest pain or significant ECG changes, thus supporting the theory of distal microembolization as a cause of myonecrosis.

- DM, smoking, and elevated serum lipids were independent predictors of post PCI troponin-I elevation, and thus were indicators of need for revascularization.

Summary

Percutaneous transluminal coronary angioplasty (PTCA) is well established technique for myocardial revascularization *(Gruenzig et al., 1979).*

The aim of this study was to detect the predictors of minor myocardial injury following visually successful uncomplicated PTCA and the effect of adding stent.

The current study was conducted on 90 patients presented by chronic angina pectoris and had lone significant proximal LAD lesion prepared for PTCA or PTCA and stenting.

All patients were subjected to proper history taking, thorough clinical examination, 12 leads ECG before and after the procedure, 300 mg loading dose of clopidogrel at least 12 hours before the procedure, 10000 IU IV heparin just before the intervention, and coronary angiography followed by PCI was done with registration of angiographic and procedural variables. Cardiac Tn-I and Tn-T were measured just before the procedure then after 12 hrs and 24 hrs of procedure.

Patients with PTCA were studied versus those with PTCA and stent, the demographic, clinical, angiographic and

procedural variable were studied in correlation with elevated post PCI Tn-I.

Regarding demographic variables, age and sex had non significant relation to the elevated Tn-I, while DM, smoking and elevated serum lipids proved to correlate with elevated Tn-I, but, HTN, and obesity were non significant.

Regarding clinical, preprocedural variables, ECG, procedural 3 leads ECG monitoring and follow up ECGs all had non significant relation to elevated Tn-I, while pre and post procedural follow up ECHO demonstrated significant correlation of impaired systolic function and dimensions of left ventricle to elevated Tn-I.

Regarding angiographic variables; lesion length, and type were non significant but type B lesion, post-procedural MLD and DS% had significant relation to Tn-I.

Regarding interventional variables, the total time of balloon inflation, maximal pressure of balloon inflation, and side branch occlusion had significant relation to elevated Tn-I, but balloon diameter or number of balloon inflations proved to be non significant.

Regarding adverse cardiac events, early and follow up need for revascularization had significant correlation to

elevated Tn-I, STEMI had non significant correlation and no death occurred.

Multivariate analysis of the results proved that the strongest predictor of Tn-I elevation were dissections, side branch occlusion, DM, increased total time and/or maximal pressure of balloon inflations.

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Where:

H^+: Hypertension, DM: Diabetes Mellitus, S: Smoking, Ob: Obesity, L^+: Hyperlipidemia, FS%: Fraction Shortening percent, EF%: Ejection fraction percent, EDD: End diastolic dimension, ESD: End systolic dimension, D1 : Diameter of balloon, L1: Length of balloon, MP1: Maximal pressure of balloon inflation, N: number of inflations, T.T: Total time of balloon inflation, D2: Diameter of stent, L2: Length of stent, MP2: Maximal pressure of stent inflation, SBO: Side branch occlusion, Tn-I: Troponin – I, Tn – T: Troponin – T.

Detection Of Minor Myocardial Injury After Successful Percutaneous Transluminal Coronary Angioplasty With Or Without Stenting

Thesis

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List of Abbreviations

ACC …… American College of Cardiology
ACS …… Acute coronary syndrome
ACT …… Activated clotting time
AHA …… American Heart Association
AMI …… Acute myocardial infarction
ATP …… Adenosine triphosphate
BENESTENT …. Beltium Neitherland Stents Study
CABG …… Coronary artery bypass graft
CAD …… Coronary artery disease
CCU……Coronary care unit
CK-MB …… Creatine phosphokinase-myocardial band
CPK …… Creatine phsophokinase
CTn-I …… Cardiac troponin-I
CTn-T …… Cardiac troponin-T
CTn-C …… Cardiac troponin-C
CTO …… Chronic total occlusion
DCA …… Directional coronary atherectomy DS Distance of stenosis
DS …… Distance of stenosis
ECG …… Electrocardiography
ECHO …… Echocardiography
EDD …… End diastolic dimensions
ELISA …… Enzyme linked immunosorbent assay
ESC……...European Society of Cardiology
ESD …… End systolic dimensions
HFABPs …… Heart fatty acids binding proteins
IVUS …… Intravenous ultrasonography
LAD …… Left anterior descending artery
LAO …… Left anterior oblique

List of Abbreviations (Cont.)

LCX ····· Left circumflex artery

LD ····· Lactate dehydrogenase

LMCA ····· Left main coronary artery

MHC ····· Myosin heavy chains

MLC ····· Myosin light chains

MLD ····· Minimal lumenal dimensions

PCI ····· Percutaneous coronary intervention

PDA ····· Posterior descending artery

PMI ……..Periprocedural myocardial injury

PTCA ····· Percutaneous transluminal coronary angioplasty

QCA ····· Quantitative coronary analysis

RAO ····· Right anterior oblique

RCA ····· Right coronary artery

STEMI…….. ST segment elevation myocardial infarction

STRESS ····· Stent restenosis study

TEA ····· Transluminal extraction atherectomy

ULN…….. Upper limit of normal

Introduction and Aim of the Work

Review of Literature

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Arabic Summary

قَالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم

سورة البقرة آية (32)