Review of Electrocardiography on Inferior Wall Myocardial Infarction

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JIM and LAU: ***Review of Electrocardiography on Inferior Wall Myocardial Infarction.*** *Inferior wall myocardial infarction is a very interesting clinical entity. Apart from different extent of left ventricular infarction, it may present with concomitant right ventricular or atrial infarction. In addition, it is also associated with high incidence of brady- and tachy-arrhythmias. The infarct-related artery can either be the right coronary, left circumflex, or even left anterior descending artery. The short-term prognosis is greatly affected by the development of these complications. ECG is an indispensable tool for the management of this clinical condition. This review concisely illustrates the basic principles of ECG, and gives a brief summary on the diagnostic, topographic, and prognostic value of ECG on the clinical management of inferior wall myocardial infarction. (J HK Coll Cardiol 2007;15:12-31)*

Acute myocardial infarction, electrocardiography, ST-segment elevation

摘要

下壁心肌梗塞是一種有趣的疾病。除了不同程度的左心室梗塞外，它還可以同時表現爲右心室或心房的梗塞。除此之外，它還可伴隨高發生率的慢速心律失常和快速心律失常。發生梗塞的動脈可以是冠狀動脈右支、左旋支、或是左前降支。近期預後很大程度上取決於這些併發症的發展。心電圖是處理這類臨床病症必不可少的工具。本綜述簡要地說明了心電圖的基本原理，並對下壁心肌梗塞的診斷、局部解剖、和心電圖對臨床治療預後的判斷作了簡要的總結。

關鍵詞：急性心肌梗塞　心電圖　ST段抬高

Introduction

Coronary artery disease is endemic in developed countries, and is the leading cause of mortality in the United States. In Hong Kong, 4460 patients suffered from acute myocardial infarction (MI) and 1558 (34.9%) of them died in 2001. The number of patients who suffered and died from heart diseases per year increased from 2,103 to 4,028 between 1981 and 2004. The increase is nearly two-fold (Figure 1).[1]

It has been suggested that inferior wall MI is clinically more benign than anterior wall MI.[2] However, some specific patient subsets, for instance, those with right ventricular infarction or complete atrio-ventricular

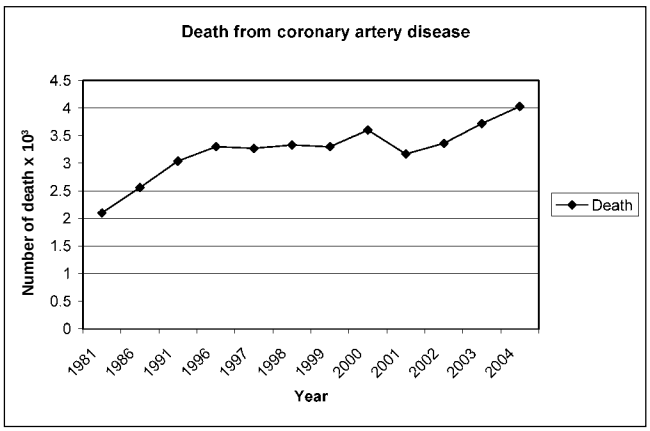

Figure 1. *Death caused by coronary artery disease from 1981 to 2004 in Hong Kong.*

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block are prone to increased in-hospital mortality. Compared with anterior wall MI, inferior wall MI presents with more challenge in ECG appearance: concurrent ischaemia of other cardiac structures in addition to the left ventricular infarction; involvement of at least two possible culprit vessels; and is associated with high incidence of atrial and conduction system arrhythmias. These clinical variations intermingle with each other and may affect the short- and long-term outcomes.

Inferior wall MI is due to sudden occlusion of one of the major coronary arteries, causing transmural infarction of the inferior myocardium. Clinically, it is defined as typical chest pain of longer than 30 minutes; ST-segment elevation of ≥1.0 mm in ≥two inferior leads (II, III, aVF); and more than twofold increase in serum creatinine phosphokinase (CPK) level. A new definition of MI has been published by the Joint European Society of Cardiology/American College of Cardiology Committee[3] (Table 1). The culprit artery is the right coronary artery (RCA) in majority of cases (80%), followed by the left circumflex artery (LCX) (20%), and rarely the left anterior descending artery (LAD) from which it is usually seen in combination with anterior wall MI. The RCA, unlike the LAD and LCX which predominantly supply the left ventricle, supplies various branches to different vital structures along its path (Figure 2). The resultant clinical presentation depends on the level of obstruction. Thus, atrial infarction, right ventricular infarction, supra-ventricular tachyarrhythmias and bradyarrhythmias can accompany the ventricular infarction. On the contrary, the LCX is relatively simple and gives blood supply to the left atrium and posterolateral wall by the recurrent atrial branch and obtuse marginal (OM) branch, respectively. The infarct size, disease course, and subsequent clinical outcomes are determined by the site of occlusion as well as the relative dominance of the culprit vessel.

ECG

ECG is an essential and the one of the most valuable tools for the diagnosis and management of inferior wall MI. In the resting state, the cardiac myocytes have a negative trans-membrane potential (electrical potential inside the cell relative to extracellular space). On stimulation, the cell membrane becomes porous and allows positive ions to move inside the cell. As a result, the polarity of the trans-membrane potential is reversed; the cell membrane becomes depolarized. The shape of an action potential of a cardiac myocyte is composed of five phases and shown in Figure 3. This depolarizing current advances towards other

Table 1. New definition of MI published by the Joint European Society of Cardiology/American College of Cardiology Committee[3]

Definition of acute, evolving, or recent MI:

1) Typical rise and gradual fall (troponin) or more rapid rise and fall (CK-MB) of biochemical markers of myocardial necrosis with at least one of the following:
   a) ischaemic symptoms;
   b) development of pathologic Q waves on the ECG;
   c) ECG changes indicative of ischaemia (ST-segment elevation or depression); or
   d) coronary artery intervention (e.g., coronary angioplasty).
2) Pathologic findings of an acute MI.

Definition of established MI:

1) Development of new pathologic Q waves on serial ECG. The patient may or may not remember previous symptoms. Biochemical markers of myocardial necrosis may have normalized, depending on the length of time that has passed since the infarct developed.
2) Pathologic findings of a healed or healing MI.

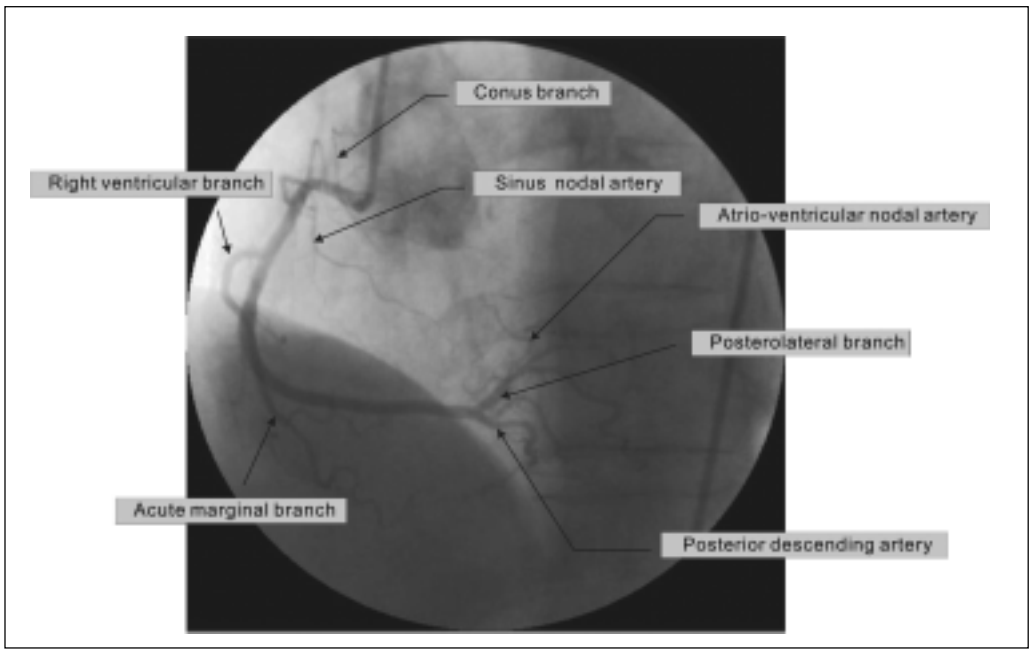


Figure 2. *Right anterior oblique view showing the RCA and its branches.*

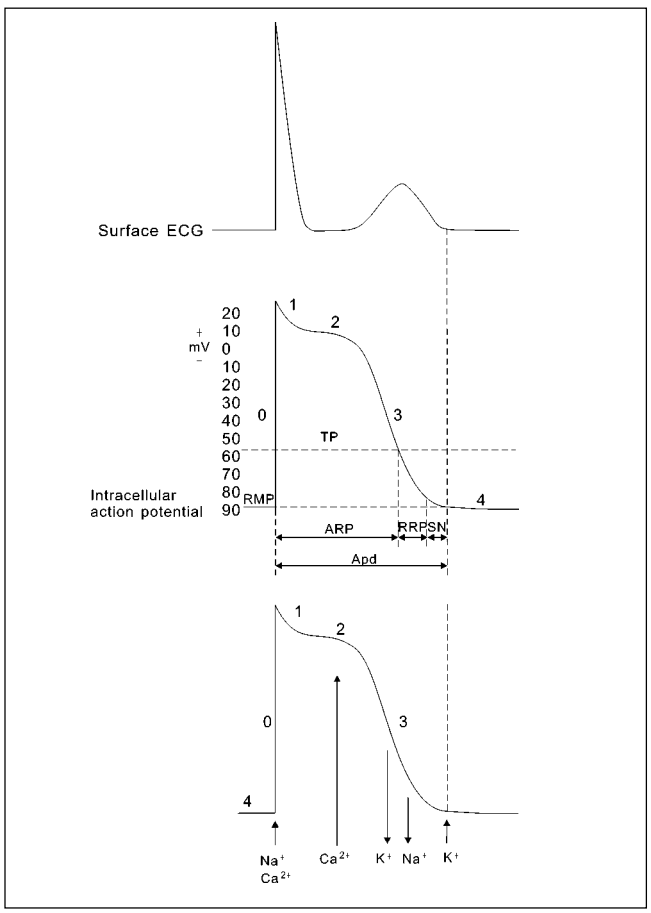


Figure 3. *Diagrams showing the transmembrane potential and movement of ions during an action potential.*

un-depolarized area within the same cell, then spread to adjacent cells through gap junctions. By this means, simultaneous recruitment of small currents from many cardiac myocytes forms a depolarizing front that sweeps across the whole heart. The electric current then continues to radiate out to the surrounding structures, which in turn modify its electrical characteristics. These minute electrical activities on the body surface are synthesized into a 12-lead ECG.

While standard ECG interpretation is a routine medical practice, some special leads relevant to the topic of the thesis are summarized. Apart from the standard limb and chest leads, right precordial $V_{1\text{-}6\,R}$ and posterior leads $V_{7\text{-}9}$ are sometimes needed to increase the sensitivity of detection and assessment of the extensiveness of ischaemia, in suspected inferior wall MI. The standard lead connection is shown in Figure 4. The limb and chest leads look at the depolarization on a frontal and horizontal plane, respectively. A positive deflection indicates the direction of current flow is towards the lead, and vice versa. The mean electrical axis θ can be simply calculated from the ratio of the area under the waveform in lead aVF and I by using the formula tan θ = aVF/I (Figure 5).

At each cardiac cycle, three waveforms, two segments and three intervals are recorded which form

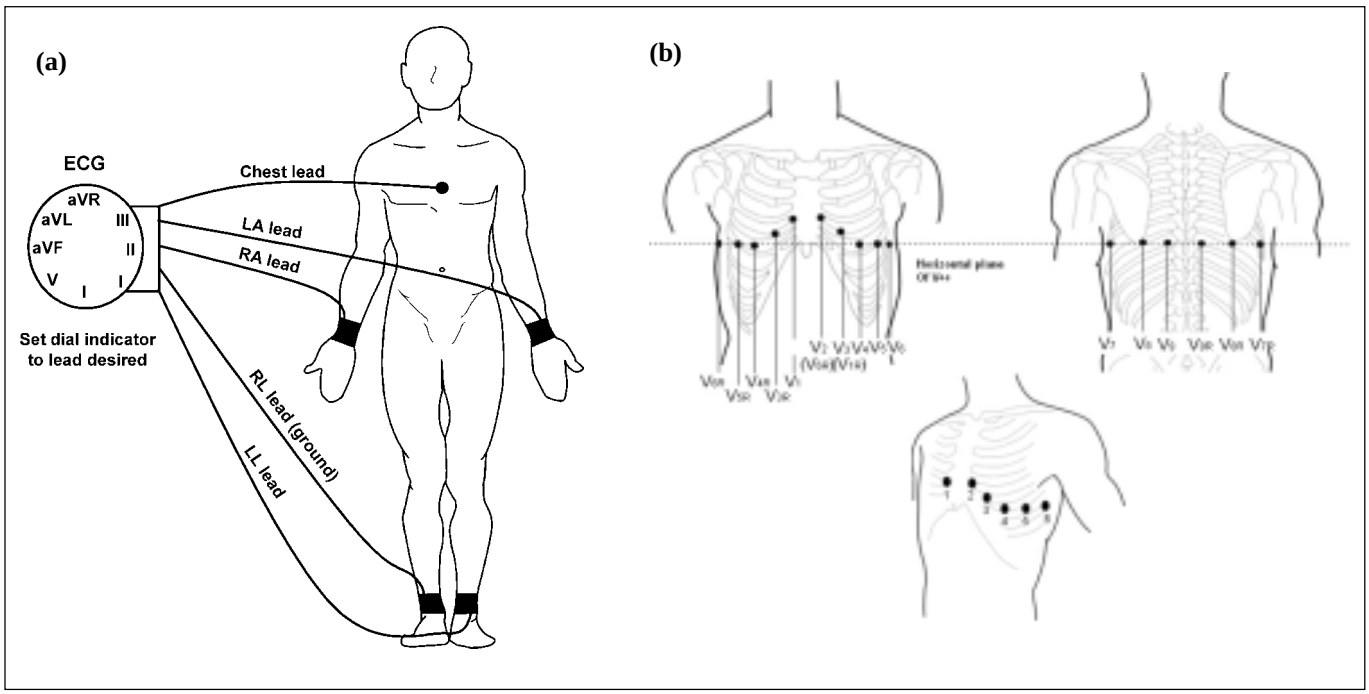


Figure 4. *(a) Standard limb lead connections; (b) Standard chest lead, right precordial lead, and posterior lead connections.*

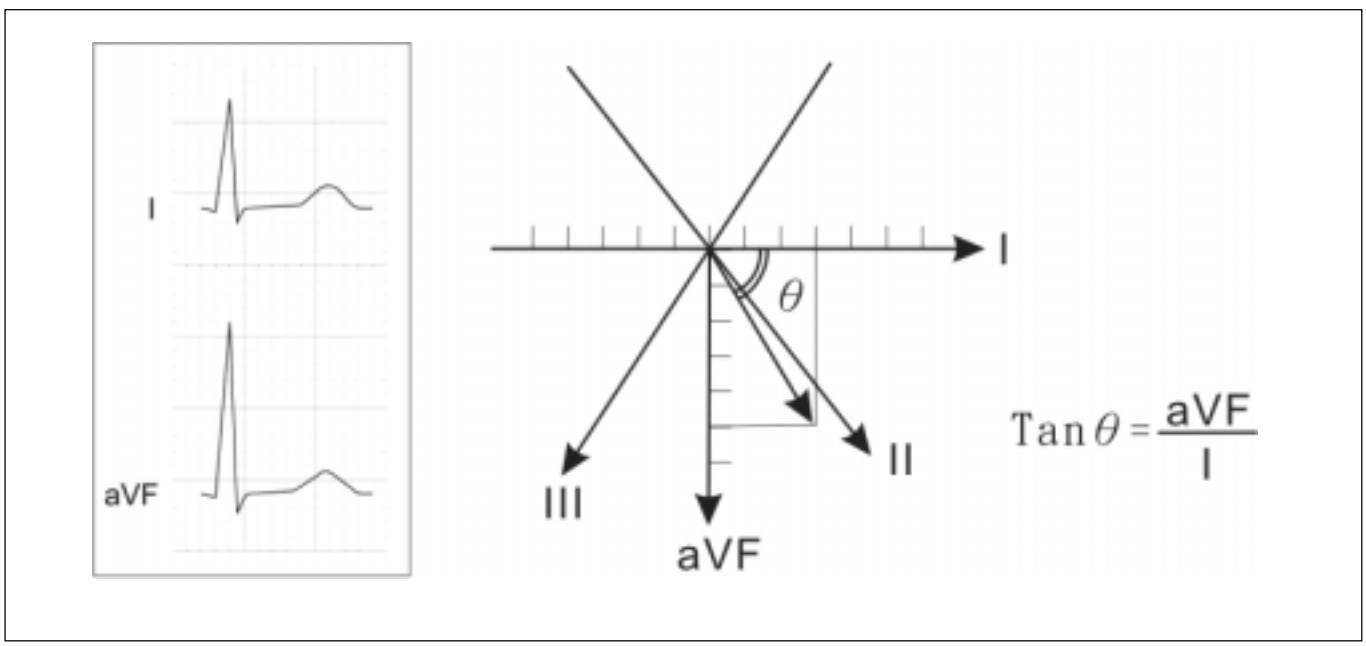


Figure 5. *A simplified method of QRS-axis calculation.*

the basic components of a normal ECG (Figure 6). The P wave indicates depolarization of the atria, the normal P wave axis lies between +30° and +75° in 96% of healthy people. The normal vector is directed downward and to the left, producing an upright P wave in lead I, II, aVF and V_{4-6}. The P wave may be bifid in lead II and biphasic in lead V_1. The P wave width is normally <110 ms in lead II. Left atrial enlargement produces a broad (≥110 ms), and notched (≥40 ms from peak to peak) P wave in lead II and a large negative component (≥ 0.4 mm sec) in lead V1. Right atrial enlargement is indicated by a tall P wave of >1.5 mm in lead V_1 or V_2. It is usually accompanied by right axis deviation.

The PR-segment is the isoelectric region beginning with the end of P wave and ending with the onset of the QRS complex. It represents the time required for impulse to travel through the atrio-ventricular node and the His-Purkinje system. The normal PR-interval ranges from 120 ms to 200 ms as measured in the limb leads. Prolongation of PR-interval implies various degrees of atrio-ventricular block. The PR-segment also overlaps with the period of atrial repolarization, whose voltage change is usually too small to be detected. Any abnormal atrial pathology may also be represented by PR-segment deviation.

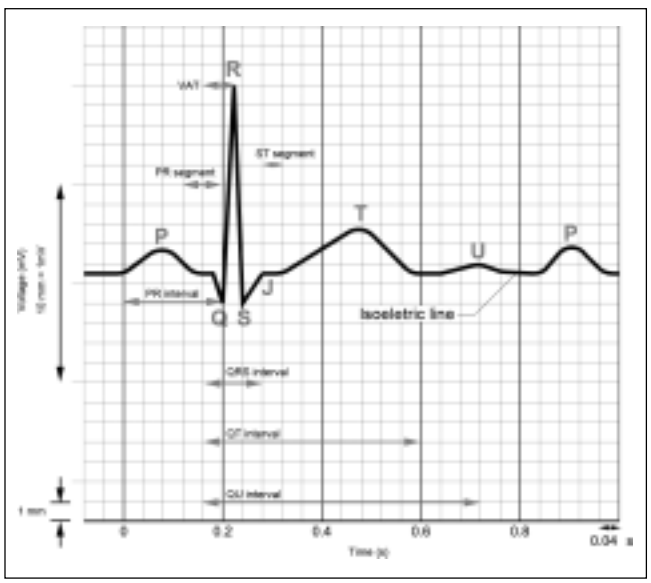


Figure 6. *A normal ECG.*

P wave is followed by a steep QRS complex which marks the ventricular activation. Ventricular excitation is the product of two temporally overlapping functions, endocardial (through His-Purkinje system) and transmural activation (through muscular conduction). Q wave is the initial negative deflection due to activation of the septum by a current flow from left to right; R wave is the first positive deflection caused by activation of main bulk of the left ventricle; and S wave is the first negative deflection after a positive wave, caused by delayed activation of the left posterior wall. The QRS complex terminates at the J point where it continues as the ST-segment. This is finally followed by T wave which denotes ventricular repolarization. During the repolarization process, ions move in opposite directions with respect to depolarization so that the resting transmembrane potential is slowly restored. As a general rule, the first cell to depolarize is the first to repolarize; hence the repolarization front spreads from the apex to the base of the heart. This results in a positive, asymmetrical T wave with a gentle slope.

The physiologic Q wave width is normally <30 ms at lead I or aVL. As a general rule, septal Q waves are seen in leads with tallest R waves. The presence of Q waves in lead 90° from the QRS axis suggests pathologic Q waves. However, wide Q waves in lead aVL, or III do not necessarily represent infarction. Abnormal Q wave (>40 ms) is a recognized sign of myocardial necrosis; the exact underlying electrophysiological mechanism is unclear. Early appearance of Q waves in acute MI may reflect irreversible damage or a large ischaemic zone.[4,5] Other investigators found that at the very early stage of acute MI, Q waves may not represent irreversible myocardial damage and should not preclude thrombolytic therapy. Indeed, Q waves may be transient in the course and disappear after thrombolytic therapy, particularly in precordial leads in anterior wall MI.[6] Interestingly, Q waves sometimes develop rapidly only after reperfusion, especially in inferior wall MI.[7]

The normal range for the mean QRS axis in adults is from -30° to +120°. In the absence of bundle branch block, an abnormal axis is a marker of structural heart disease. The QRS axis can be estimated by from the

R waves in lead I, II, and III. Left axis deviation is hinted by positive R wave in I, negative or biphasic R wave in II, and negative R wave in III. Right axis deviation is indicated by negative R wave in I and positive R waves in II and III. The duration of QRS complex is normally <120 ms. Prolongation of QRS complex (≥120 ms) suggests either a left or right bundle branch block, or non-specific intra-ventricular conduction delay. In the setting of acute MI, the intense ischaemia can distort the terminal portion of the QRS complex, depends on the degree and extent of ischaemia. The grading of ischaemia is shown in Figure 7.

Grade I ischaemia is characterized by symmetrical, tall T waves. Grade II ischaemia is ST-segment elevation without distortion of the terminal portion of the QRS complex. Grade III ischaemia is distortion of the terminal portion of QRS complex with loss of S waves and J/R wave ratio ≥50%.[8,9] Grade III ischaemia is associated with larger final infarct size, less myocardial salvage by thrombolytic therapy, a more rapid progression of necrosis over time and higher mortality.[10] Grade III morphological change is explained by prolongation of electrical conduction in the Purkinje fibers in the ischaemic region. The delayed conduction decreases the degree of cancellation, resulting in an increase in R wave amplitude and a loss of S wave. Since the Purkinje fibers are very resistant to ischaemia, terminal QRS distortion is probably only seen in severe and prolonged ischaemia.[11] In patients who have collateral circulation, no changes are detected in the QRS complex during prolonged balloon angioplasty.[12]

The ECG change of grade III ischaemia has a marked resemblance with the giant R wave described in Prinzmetal's angina[13] and early phase of acute MI,[14] especially in the setting of variant angina during treadmill testing,[15,16] unstable angina, variant angina with progression to acute MI, percutaneous coronary angioplasty during balloon occlusion,[17] or experimental ligation of coronary artery in animal laboratory.[18,19] Giant R wave is characterized by greater than 50% increase in the amplitude of R wave, disappearance of S wave, merging of the QRS complex with the ST-segment causing a wide and bizarre-shaped, monophasic QRS-ST complex. Sometimes, it can be mistaken as bundle branch block or even ventricular tachycardia if it co-exists with fast heart rate, which tends to obscure the preceding P wave. It is usually found in leads where there is maximal ST-segment elevation (leads that facing the area of maximal ischaemia) and more common in anterior, rather than inferior MI.[20] QRS-axis deviation is invariably found, with left axis deviation associated with anterior MI, and right axis deviation with inferior MI. In the acute phase of ischaemia, the giant R-wave has convex ST-segment elevation and T wave inversion. However, on amelioration of the ischaemia, the amplitude of R wave is attenuated, the ST-segment elevation becomes concave and T wave returns to upright.[21]

The ST-segment begins with the end of S wave and ends with the onset of T wave. It is of great clinical importance in the diagnosis of acute MI. In ischaemic cells, the resting trans-membrane potential is less negative and the positive potential during the plateau phase is less positive compared with normal cells (Figure 8). As a result, injury current flows away from at phase 0 (diastole) and towards the ischaemic zone at phase 3 (systole). This phenomenon produces simultaneous TQ-segment depression and ST-segment elevation in the ischaemic area. After auto-compensation of baseline shift by the ECG machine, it finally presents

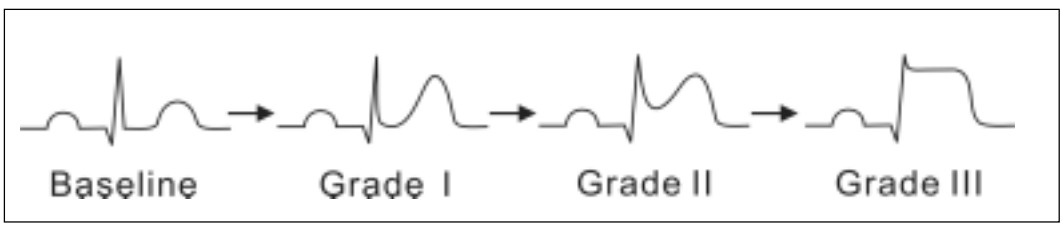


Figure 7. *The grading of ischaemia in leads with baseline qR configuration.*

as marked ST-segment elevation. By the same token, injury current flows from epicardial side towards the endocardial side in subendocardial infarct, which will then present as ST-segment depression (Figure 9).

Apart from diagnostic and topographic functions, ST-segment is also useful in the initial risk stratification and subsequent monitoring of treatment response in patients with acute MI. The total sum of ST-segment elevation in inferior leads (for inferior MI) and the total number of leads with ST-segment elevation in precordial leads (for anterior MI) has been used to predict infarct size.[22,23] After early reperfusion of the infarct-related artery by thrombolysis or primary angioplasty, ECG usually shows rapid ST-segment resolution. ST-segment resolution of ≥50% measured at 90 minutes from the initiation of thrombolysis correlates well with infarct-related artery patency.[24] However, the absence of ST-segment resolution does not accurately predict an occluded vessel. Approximately 50% of patients who have no (≤30%) ST-segment resolution still get a patent infarct-related artery.[25,26] The measurement of ST-segment resolution can be done on a single lead with maximal ST-segment elevation or by calculating the sum of the total ST-segment of all 12 leads. It seems that the latter method is more useful for patients who have small ST-segment elevation. Reperfusion is a dynamic process which is characterized by repeated cycles of re-occlusion and recanalization, continuous ECG monitoring is thus preferable to intermittent recording since one could not confidently differentiate a partial ST-segment resolution from a complete resolution followed by re-elevation. Patients who have inferior wall MI develop significantly more ST-segment resolution than those of anterior wall MI,[27] it has been suggested that ≥70% ST-segment resolution may be more optimal for inferior wall MI, whereas ≥50% ST-segment resolution is kept for anterior wall MI. The preservation of left ventricular function by reperfusion therapy depends on myocardial tissue perfusion, rather than the infarcted epicardial artery patency. Various studies have shown that ST-segment resolution of ≥70% is an indicator of myocardial tissue perfusion.[28,29] In conjunction with angiographic parameters such as myocardial blush score or corrected Thrombolysis In

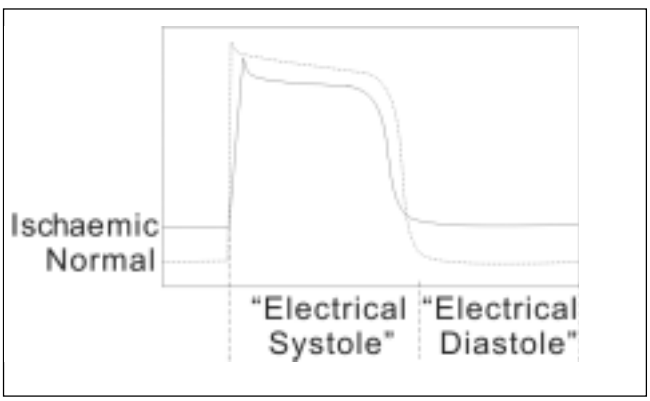


Figure 8. *The difference in shape of action potential between a normal and ischaemic cell.*

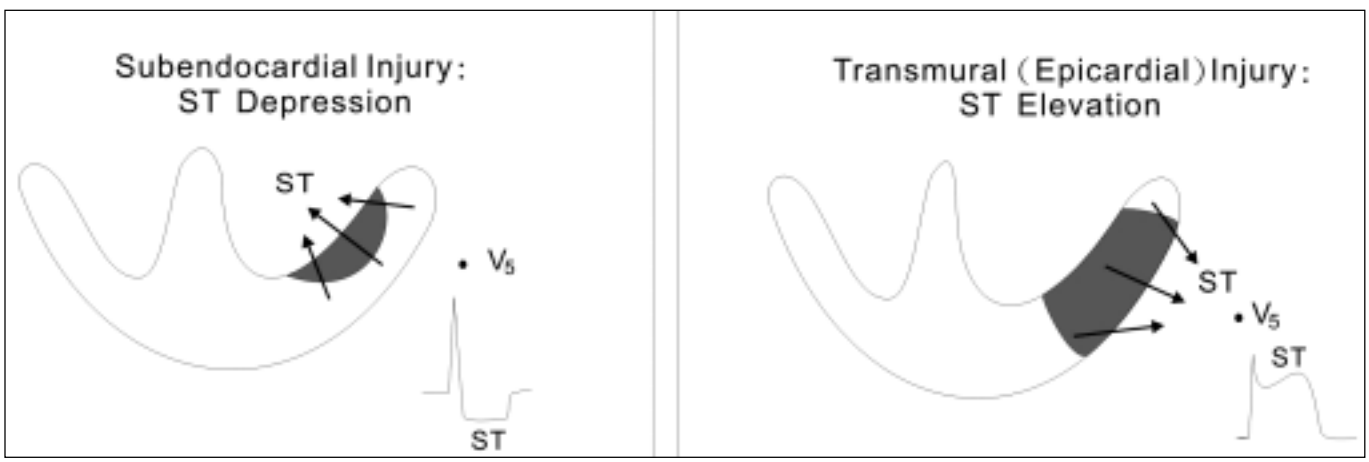


Figure 9. *Current-of-injury pattern with acute ischaemia. The left panel represents subendocardial ischaemia, the vector is directed towards the inner layer of the affected ventricle. Overlying ECG records ST-segment depression. The right panel represents the transmural infarction, the vector is directed outward. ECG thereby showed ST-segment elevation.*

Myocardial Infarction (TIMI) frame count, ST-segment resolution in inferior wall MI have been shown to predict left ventricular function.[28]

During the course of acute MI, the T wave undergoes an evolutionary change of peaked and upright T wave in acute phase, followed by T wave inversion in the first week. The magnitude of T wave inversion decreases gradually and becomes upright again in the weeks following. Early inversion of terminal portion of T wave after initiation of thrombolytic therapy is an indicator of reperfusion success.[30] Corbalan, et al.[31] found that inversion of T wave more than 0.5 mm below the baseline within 24 hours of thrombolytic therapy in all leads with previous ST-segment elevation has been associated with reperfusion and lowest mortality. However, T wave inversion developed in the initial ECG before thrombolytic therapy in patients who were admitted between two to six hours from the onset of chest pain was associated increased mortality.[32] One could not tell whether this signifies spontaneous reperfusion (better prognosis) or accelerated myocardial necrosis (poor prognosis). Early reversion to upright from inverted T wave indicates either post-infarct pericarditis or re-infarction.

Diagnosis

Atrial Infarction

In general, atrial infarction is usually overlooked because of its subtle ECG changes, uncertain clinical and prognostic significance, and over-dominance of clinical picture by the accompanying ventricular infarction. The salient clinical features and complications of atrial infarction are summarized in Table 2. Atrial infarction can be associated with increased morbidity and mortality.[33,34] Supra-ventricular tachyarrhythmias occurred in 61-74% of patients,[35] and in the presence of loss of atrial kick caused by atrial infarction, it can significantly compromise cardiac output and worsen the prognosis. Urgent cardioversion may be indicated. Intra-atrial thrombosis was found in over 80% of cases, and predisposed to thrombo-embolism. Indeed, pulmonary and peripheral artery embolism was present in 24% of autopsy-proven cases of atrial infarct. Atrial rupture carries a grave prognosis and occurred in 4.5% in one autopsy series.[36] The onset is usually within 24 hours, although delayed onset had been reported. The question of anti-coagulation is thus a matter of controversy.

The incidence of atrial infarction ranged from 1-42% of patients who died from acute MI.[37-39] Because the atrium is a thin-walled structure, post-mortem examination invariably showed transmural infarct, involving the area around the atrio-ventricular groove. The right atrium was involved in majority of cases (81-98%) with the right atrial appendage mostly affected, followed by biatrial involvement (19-24%) and left atrium (2-19%) alone.[37,39,40]

To date, ECG is the only means of antemortem diagnosis of atrial infarction. The electrical criteria were derived from early experimental studies of the ECG changes on ligation of atrial branch in animals,[37,41,42] or from retrospective ECG analysis of autopsy-proven cases.[43,44] PR-segment deviation, changes in P wave contour and supra-ventricular dysrrhythmias are three principle features associated with atrial infarction.[45] By vector analysis, the direction of the PR-segment

Table 2. Clinical and ECG characteristics of atrial infarction

	Incidence
ECG findings	
Supra-ventricular dysrrhythmias	
Atrial fibrillation	33-55%
Atrial flutter	9%
Other atrial dysrrhythmias	6-17%
Wandering atrial pacemaker	4%
Sinus arrest	4%
Atrio-ventricular block	6%
PR-segment deviation	
Elevation	8%
Depression	16%
Abnormal P wave morphology	Uncertain
Complications	
Supra-ventricular dysrrhythmias	61-74%
Atrial rupture	4.5%
Intra-arterial thrombosis	80-84%
Pulmonary or peripheral embolism	24%

displacement is always towards the area of the atrial infarct. Thus, PR-segment depression is equivalent to ST-segment elevation in ventricular infarct. Burch, et al.[46] summarized his 30-year experience in this field and made a statement that PR-segment depression of a "fraction" of a millimeter or more was associated with atrial infarction in 100% of cases. Liu, et al.[47] reviewed previous clinical and experimental studies and proposed a new criteria for atrial infarction which gained wide acceptance (Table 3). Attempt was made to differentiate between left and right atrial infarct but no consensus had been reached. Jim, et al.[48] described an atypical ECG finding of PR-segment elevation of 0.5 mm in inferior leads. He suggested it might represent a case of isolated left atrial infarct since the left atrium is a posterior structure with respect to the right atrium which is commonly affected.

The diagnostic accuracy of these criteria for atrial infarction remains unknown. No other test is accurate enough to verify their sensitivities and specificities, which are probably low. All the studies so far were autopsy series, no clinical study has been conducted on this clinical entity. It appears that PR-segment deviation of a certain cut-off point is needed to define the population at risk of developing complications, as well as to predict patients' prognosis.

Right Ventricular Infarction

Right ventricular infarction was thought to be a clinically insignificant entity as no adverse hemodynamic effect was demonstrated in animal models.[49,50] Its importance started to be recognized only after the classical syndrome of hypotension, clear lung fields and raised jugular venous pressure was described by Cohn, et al.[51] Right ventricular infarction is predominantly a complication of inferior wall MI, which is seen in 30% to 50% of these patients.[52] About one half of the right ventricular infarct become hemodynamically compromised. It is generally believed that right ventricular infarction is precipitated by proximal occlusion of RCA, causing infarction of the anterolateral wall of the right ventricle, which is supplied by the right ventricular branch and acute marginal branch. However, while proximal occlusion of RCA increases the likelihood of right ventricular infarction, autopsy series showed that the posterior right ventricular wall is always involved, with frequent association of left posterior wall and posteroseptal wall infarction.[53,54] This finding explains the observation that right ventricular infarction sometimes occurs in distal RCA and LCX occlusion. The right ventricle possesses intrinsic properties that protect it from ischaemic injury. For examples, the lower oxygen requirements of right ventricle due to its smaller muscle mass (one sixth of that of left ventricle) and work load (one fourth of that of left ventricle), blood supply that occurs both during diastolic and systolic filling, collateral flow from the left coronary circulation, and direct diffusion of oxygen from intra-cavitary blood to the thin walls of the right ventricle.

Inferior wall MI with concomitant right ventricular infarction was associated with increased in-hospital complications, such as cardiogenic shock, atrial fibrillation, complete atrio-ventricular block and ventricular fibrillation (64% vs. 28%, $p<0.0001$), and a higher mortality (31% vs. 6%, $p<0.0001$) compared with inferior MI alone.[52] Prompt reperfusion of right ventricular branch by primary angioplasty results in recovery of right ventricular function and improved mortality (2% vs. 58%, $p=0.001$).[55] Therefore, it is clinically important to identify this high-risk subset.

The diagnosis of right ventricular infarction can

Table 3. Liu's diagnostic criteria of atrial infarction[47]

Major criteria

1. PR-segment elevation >0.5 mm in leads V_5 and V_6 with reciprocal PR-segment depression in leads V_1 and V_2.
2. PR-segment elevation >0.5 mm in lead I with reciprocal depression in leads II and III.
3. PR-segment depression >1.5 mm in precordial leads and 1.2 mm in leads I, II and III in associated with any atrial arrhythmias.

Minor criteria

1. Abnormal P waves: M-shaped, W-shaped, irregular, or notched.

be made by many tools, and the diagnostic criteria of these investigations are summarized in Table 4. Among them, ECG is the most accurate and easily accessible method. ST-segment elevation of ≥ 1.0 mm in lead V_{4R} is a reliable sign of proximal RCA occlusion[56] (sensitivity 100%, specificity 87%) and right ventricular infarction[52] (sensitivity 88%, specificity 78%). Because the right ventricle is also supplied by other vessels, any RCA occlusion distal to the first right ventricular branch may still cause right ventricular infarction. This accounts for the relatively suboptimal specificity. In addition, as right precordial leads is not routinely performed in all emergency room, and as such ECG changes may last only for a short period of time, some cases of right ventricular infarction occur undetected. Braat, et al.[57] found that 48% of the ST-segment change resolved within 10 hours. More importantly, in case of proximal occlusion of a very dominant RCA, the presumed presence of ST-segment elevation in V_{4R} can be masked by concurrent posterior left ventricular wall ischaemia which depresses the ST-segment in right precordial leads.[58]

In inferior wall MI, the direction of injury current is predominantly downward (inferior-pointing). When there is concomitant right ventricular infarction, it shifts direction more to the right and anterior. Thus, significantly more ST-segment depression (reciprocal change) in lead aVL and ST-segment elevation in lead V_1 is expected. Turhan, et al.[59] found that ST-segment elevation of ≥1.0 mm in lead aVL was sensitive (87%) and specific (91%) in prediction of right ventricular infarction. Fiol, et al.[60] found that isoelectric or ST-segment elevation in lead V1 was fairly sensitive (70%)

Table 4. Different diagnostic criteria for acute right ventricular infarction

Authors	Tool	Criteria	Sensitivity	Specificity
Dell'Italia, et al. (1983)	Physical examination	Hypotension, clear lung field and raised jugular venous pressure	25%	N/A
		Dilated neck veins	88%	69%
Cohn, et al. (1974)	Hemodynamics	Right atrial pressure > pulmonary-capillary wedge pressure	N/A	N/A
Lopez-Sendon, et al. (1981)		Right atrial pressure >10 mmHg and right atrial pressure/ pulmonary-capillary wedge pressure ≥0.8	73%	100%
		y-descent deeper than x-descent	55%	97%
Sharpe, et al. (1977)	Echocardiography	RV/ LV (end-diastolic dimension)	N/A	N/A
Bellamy, et al. (1986)		RV dilatation and asynergy + abnormal interventricular septal motion at short-axis	82%	93%
Braat, et al. (1983)	ECG	V_{4R} ST-segment elevation of ≥1.0 mm	93%	93%
Croft, et al. (1982)			90%	91%
Tobinick, et al. (1977)	Scintigraphy	RVEF <40%	N/A	N/A
Rigo, et al. (1975)		RV area/LV area >2	N/A	N/A
Dell'Italia, et al. (1984)		RVEF <40% + RV motion abnormality	92%	82%

RV = right ventricle, LV = left ventricle

and specific (87%) in predicting proximal RCA occlusion. Moreover, the sum of ST-segment depression in lead I and aVL of ≥5.5 mm adds more specificity compared with ST-segment depression of ≥1.0 mm in aVL (91% vs. 72%).

Takotsubo Cardiomyopathy

Takotsubo cardiomyopathy or transient left ventricular apical ballooning syndrome was first described in Japan in 1991.[61] In recent few years, it has been increasingly recognized and reported in Europe and North America.[62-64] The syndrome is characterized by transient and severe dysfunction involving the mid-ventricle and apical segments with hyperkinesis of the basal segments of the left ventricle, producing a typical morphology of a "takotsubo", which is a fishing pot with round bottom and narrow neck used for trapping octopus in Japan. It usually affects post-menopausal women, and is commonly preceded by various emotional and physical stresses. Patients typically present with either chest pain or dyspnoea. ECG invariably shows precordial ST-segment elevation, evolutionary T wave abnormalities, or Q waves. ST-segment elevation in inferior leads has also been reported in few cases. Cardiac enzymes are only mildly elevated. The clinical picture is indistinguishable from acute coronary syndrome. Coronary angiography reveals completely normal coronary anatomy or minor coronary artery disease in most of the cases. The left ventricular ejection fraction on admission ranges from 20-49%, the extent of the left ventricular involvement is beyond the distribution of a single epicardial coronary vessel. Right ventricular involvement has been reported and verified by MRI.[65] The disease carries a good prognosis on conservative treatment. The left ventricular dysfunction improves rapidly within days or weeks; the in-hospital mortality is only 1.1%.[63,66] The exact etiology remains unknown. Although multiple mechanisms has been suggested; for instance, multivessel coronary spasm, coronary microvascular dysfunction, and catecholamine-mediated cardiotoxicity, no single hypothesis is compelling. Spontaneous and provocable multivessel spasm has been identified in only 1.4% and 28.6% of patients, respectively.[62] The causal role of catecholamines is suggested by case reports of the association of the disease in pheochromocytoma,[67] or after adrenaline infusion (iatrogenic).[68] Indeed, plasma catecholamine level has been found two to three times higher than control patients with acute MI.[64] In animal models, the disease could be prevented by combined blockade of α- and β-adrenoceptors but not by direct vasodilators.[69]

A variant form of the disease has been described by Haghi et al.[70] The basic clinical characteristics are very similar except that the basal and mid segments are hypokinetic while the apex is spared. These features clearly speak against an epicardial coronary aetiology, in which case the apex should be more affected. Sympathetic nerve plexus and fibers are normally more densely distributed in basal segments than in the apex. Increased adrenoceptor density in cardiac apex and increased apical myocardial responsiveness to adrenergic stimulation are postulated to be the underlying causes of the syndrome.[71]

Early recognition of this condition will avoid unnecessary thrombolysis, which is associated with a substantial bleeding risk, especially in the elderly. Suspicious cases should be sent for emergency cardiac catheterization which is the only reliable means to distinguish it from acute coronary syndrome. Cautious analysis and interpretation of readily available diagnostic tools, such as ECG and echocardiography, is thus essential for arousing the initial clinical suspicion. The ECG characteristics of the syndrome have yet been well defined. While most of the reports have incriminated the anterior left ventricular wall in the syndrome, it is entirely possible that the inferior wall MI pattern may occur if the inferior neuro-cardiac plexus are involved.

Topography

The topographic distribution of ST-segment deviation in an ECG is very useful for the prediction of ischaemic territory, infarct-related artery and site of thrombotic occlusion. It sometimes helps us to understand the physiology and anatomy of the coronary circulation. The leads are traditionally clustered into groups according to the myocardial region that the leads are oriented. Leads II, III and aVF are inferior leads which look at the heart from the inferior aspect; leads I

and aVL are superior leads which look at the high lateral wall; leads V_{1-4} look at the septum and apex; leads V_{5-6} look at the apex and lateral wall; leads V_{7-9} (posterior leads) look at the posterior wall; lead V_{4R} is the representative right precordial lead which looks at the right ventricular free wall. Traditionally, the lead groups are named with respect to their positive directions. On the other hand, the lead group are also at the same time oriented in their negative directions, i.e. their opposite walls. Thus, the lead groups are able to tell us information regarding to two rather than one myocardial regions. The direction and magnitude of ST-segment deviation in one particular lead group is determined by the vector sum of its positive and negative directions. It is the principle underlying the phenomenon of reciprocal ST-segment changes. Cancellation and augmentation of ST vectors should be considered when interpreting the site of MI.

Leads V_{1-4}

Lead V_1 is located at the right paraseptal area. Although it is categorized as one of the precordial leads, there is a poor correlation between ST-segment elevation in V_1 and V_2 with respect to site of occlusion in acute anterior MI. One reason is due to the differential supply to the right paraseptal area from the RCA and LAD. Ben-Gal, et al.[72] was able to demonstrate a close association between ST-segment elevation in V_1 and V_{3-4R} and in patients with a small conus branch (not reaching the interventricular septum) from a normal RCA who is suffering from anterior wall MI with obstruction proximal to the first septal artery. This study suggests proved the theory that the right paraseptal region is dually supplied by the septal artery from LAD and the conus branch from RCA. When one artery is small, the other is dominant, and vice versa. Other important clinical use of lead V_1 is illustrated in the setting of inferior wall MI. ST-segment elevation in V_1 (equivalent to V_{2R}) in the presence of right ventricular infarction implicates a large infarct size.[73]

Leads V_{1-4} are very interesting and intriguing. They are oriented at the interventricular septum and able to pick up ischaemic changes present on either side of the septum. Anterior wall MI typically manifests as ST-segment elevation in V_{1-6}. Interestingly, in isolated right ventricular infarction caused by occlusion of a rudimentary RCA, ST-segment elevation is predominantly found in V_{1-5}, rather than the inferior leads.[74] The total absence of inferoposterior injury in this scenario allows ECG manifestation of ST-segment elevation in the precordial leads.

Sasaki, et al.[75] studied the clinical and angiographic features of anterior wall MI with and without associated ST-segment elevation in inferior leads. They observed that the infarct size of the anterior wall MI with concomitant ST-segment elevation in inferior leads had a small infarct than with no ST-segment changes. Morphologically, the culprit LAD was usually a wrapped LAD,[76] with a distal occlusion. He concluded that the wrapped LAD brought about inferoapical wall ischaemia and ST-segment elevation in inferior leads, which would only manifest provided the occlusion is distal enough not to cause lateral wall ischaemia (less myocardium jeopardized) which tended to depress the precordial ST-segment. Sadanandan, et al.[77] conducted a similar study and got similar results from patients with acute MI accompanied by combined ST-segment elevation in anterior and inferior leads. In addition, he found that the infarct-related artery was RCA and LAD in 59% and 36%, respectively. ST-segment elevation in $V_1 \geq V_3$ and absence of progressive ST-segment elevation from lead V_1 to V_3 suggests that the infarct-related artery from the LAD. On the other hand, the ECG changes if the RCA is the culprit artery is uncertain.

Precordial leads V_{1-4} ST-segment depression is associated with larger infarct size, worse left ventricular function and outcome in inferior wall MI.[78] Such ST-segment depression may be due to pure electrical reciprocal changes,[79] concomitant LAD territory ischaemia,[80] or posterolateral infarct.[81] Subsequent studies, by means of angiography,[82,83] scintigraphy,[84] and echocardiography,[85] confirmed that concomitant posterolateral ischaemia caused by dominant RCA occlusion is the likely explanation of such ECG change. Perhaps the worst clinical outcome was found in patients who had inferior wall MI associated with maximal ST-segment depression in lead V_{4-6}. These patients tended to have global left ventricular dysfunction and higher

in-hospital mortality[86,87] despite a lower CPK leak than those with maximal ST-segment depression in V_{1-3}. Higher prevalence of LAD disease with ≥50% diameter stenosis and multi-vessel disease were found,[88-90] which accounts for the disproportionate left ventricular dysfunction and poor outcome.

Leads V_{5-6}

The clinical implication of ST-segment elevation in leads V_{5-6} in inferior wall MI is unclear. It is found more often in LCX (more lateral wall involvement) than RCA occlusion.[91] However, Assali, et al.[92] suggested that these changes were associated with occlusion of a "mega-artery", defined as an artery with a big posterolateral branch (originated from either LCX or RCA) and a small, or medium sized LAD (Figure 10). The sensitivity and specificity of detection of such a "mega-artery" was 94% and 98%, respectively. Tsuka, et al.[93] reported similar findings and a larger infarct is implicated.

Leads V_{7-9}

ST-segment elevation of ≥1.0 mm in posterior leads V_{7-9} at 80 ms from the J point is considered abnormal.[94] During angioplasty, ST-segment elevation is found in 68% of LCX but only 10% in RCA during balloon occlusion.[95] If ST-segment elevation of ≥ 0.5 mm was used, the sensitivity to detect LCX occlusion increases from 49% to 94%.[96] About 25% of LCX balloon occlusion causes ST-segment elevation in leads V_{7-9} without any ST-segment change in standard 12-lead ECG.[95] Zalenski, et al.[97] added posterior leads to the standard 12-lead ECG and found that it increased the sensitivity of detection of ischaemia in a cohort of patients presented with acute coronary syndrome.

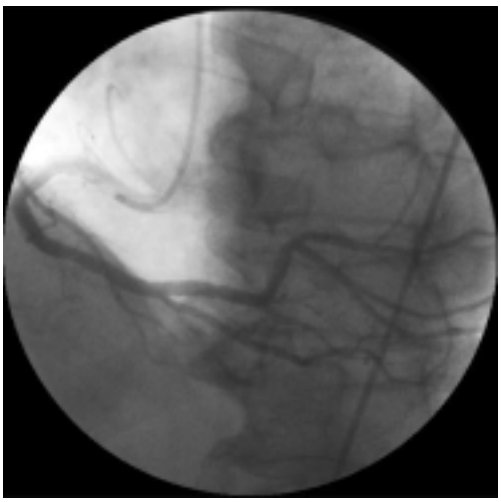


Figure 10. *Left anterior oblique view showing a RCA as a mega-artery.*

Limb and Augmented Limb Leads

The RCA supplies blood mainly to the posterior part of the septum and the inferior part of the inferoposterior wall of the myocardium, whereas the LCX supplies blood to the posterior part of the inferoposterior wall and the posterior part of the lateral wall. The vector of injury current is thus more directed to posterior and lateral in LCX occlusion. This minor difference in vector direction forms the basis of ECG differentiation between LCX and RCA occlusions. Leads III and aVF are more inferior-pointing, and thereby ST-segment elevation is found more prominent in these leads in RCA occlusion.[98] On the contrary, leads I and aVL are oriented more lateral, ST-segment depression is less prominent, or even ST-segment elevation is found in these leads in LCX occlusion.[91] In addition, the relation of the vector direction between posterior and anterior wall is more strongly opposed than that between inferior and anterior wall. Therefore, the reciprocal changes in LCX occlusion (posterior ischaemia) cause more prominent precordial ST-segment depression than that caused by changes in RCA occlusion (inferior ischaemia).[98] By applying these concepts, numerous ECG criteria have been described which predict the infarct-related artery with varying sensitivity and specificity (Table 5). Among those criteria, the ratio of ST-segment in II/ III <1 with ST-segment depression ≥0.5 mm in lead I predicts RCA occlusion, whereas the ratio of ST-segment in II/III ≥ 1 with isoelectric ST-segment in lead I best predicts RCA and LCX occlusion.[94]

Kosuge, et al.[98] described the use of a single ECG criterion to distinguish between proximal RCA, distal RCA and LCX occlusions. The ratio of ST-segment of V_3/III <0.5 predicts proximal RCA occlusion [sensitivity 91%, specificity 91%, positive predictive value (PPV) 88%, negative predictive value (NPV) 93%]; 0.5 ≤V_3/

Table 5. Sensitivity, Specificity, PPV and NPV of various diagnostic criteria for differentiation between RCA and LCx occlusions

Author	Criteria	Prediction	Sensitivity	Specificity	PPV	NPV
Chia, et al. 2000	ST ↑ II/ III =1 and ST I ↔	LCx	75%	99%	94%	93%
	ST ↑ II/ III <1 and ST ↓ I	RCA	94%	90%	97%	82%
Herz, et al., 1997	Ratio ST ↑ II/ III <1 plus ratio of ST ↓ I/ aVL <1	RCA	88%	100%	100%	97%
Assali, et al., 1998	S/R ratio >1/3 and ST ↓ >1 mm in aVL	RCA	76%	88%	96%	89%
	S/R ratio ≤1/3 and ST ↓ ≤1 mm in aVL	LCx	88%	76%	48%	96%
Wong, et al., 1995	ST ↑ V5 or V6	LCx	56%	92%	63%	89%
	ST ↓ V1	LCx	61%	84%	48%	90%
Fiol, et al., 2004	ST ↓ I ≥ 0.5 mm	RCA	92%	77%	94%	71%
	ST ↔ I	LCx	54%	92%	64%	88%
	ST ↑ I ≥0.5 mm	LCx	31%	100%	100%	85%
Nair, et al., 2002	ST ↓ ≥ 1 mm aVR	LCx	80%	96%	80%	96%
	ST ↑, ↔, or ↓ < 1 mm aVR	RCA	96%	80%	96%	80%
Bairey, et al., 1987	ST ↔ or ↑ I	LCx	83%	96%	91%	93%

ST = ST-segment, ↑ = elevation, ↔ = isoelectric, ↓ = depression

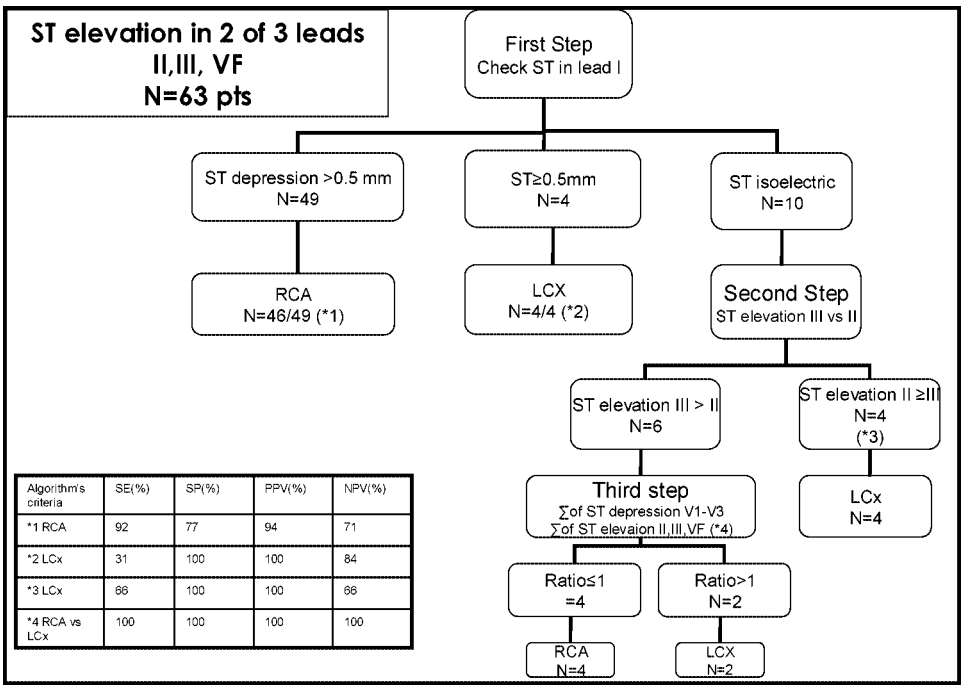
III ≤1.2 predicts distal RCA occlusion [sensitivity 84%, specificity 93%, PPV 91%, NPV 98%]; and V_3/ III >1.2 predicts LCX occlusion [sensitivity 84%, specificity 95%, PPV 73%, NPV 98%]. So far, there is a lack of effort to distinguish between proximal and distal LCX occlusion in the literature. Alternatively, Fiol, et al.[60] combined three individual criteria and produced an algorithm which was able to predict the infarct-related artery with very high accuracy (Figure 11). However, the number of patient in the study was too small to draw a definite conclusion. It is interesting to use these criteria in retrospect to deduce the initial site of occlusion in those patients who presented with inferior MI but had normal, or nearly normal coronary anatomy.

Prognosis Prediction

The ischaemic territory of inferior wall MI is of smaller size and less strategically located compared with that of anterior MI. Not surprisingly, the mortality rate of the former condition is only about half of the latter. Nevertheless, Bates[99] described three high-risk subsets of inferior wall MI patients, easily identified by ECG: (1) precordial ST-segment depression, (2) right ventricular infarction, and (3) complete atrio-ventricular block. The first two conditions have been discussed, and the occurrence of heart block, atrial fibrillation and bundle branch block are described below.

Complete Atrio-Ventricular Block

Complete atrio-ventricular block is found in 10-15% of patients suffering from inferior wall MI, the incidence remains unchanged in pre- and post-thrombolytic era.[100-102] Two-third of this conduction disturbance is developed within the first 24 hours.[102] Unlike anterior wall MI in which the extensive infarction of the septum with involvement of the bundle branches is the cause, the underlying mechanism is postulated to be either due to an increase in vagal tone (Bezold-Jarisch reflex) or accumulation of ischaemic metabolites,[103,104] evidenced by the abolition of the arrhythmia by administration atropine and adenosine antagonist (theophylline), respectively. Complete atrio-ventricular block is associated with clinical features of a larger



Algorithm's criteria	SE(%)	SP(%)	PPV(%)	NPV(%)
*1 RCA	92	77	94	71
*2 LCx	31	100	100	84
*3 LCx	66	100	100	66
*4 RCA vs LCx	100	100	100	100

Figure 11. *Sequential ECG algorithm to predict the culprit artery in inferior wall MI.*[60]

infarct, such as worse left ventricular function, cardiogenic shock, right ventricular infarction,[105] atrial fibrillation, ventricular fibrillation compared to those without.[106] Electrocardiographically, these patients have a higher total sum of ST-segment elevation in inferior leads, which implies larger infarct size.[107] In-hospital mortality is invariably higher (29% to 37% vs. 6% to 14%) compared to patients without the atrio-ventricular block.[100,108,109] Reperfusion therapy has lowered the in-hospital mortality (7% to 20% vs. 2.5% to 4%) but it is still higher than those without the atrio-ventricular block.[110,111] However, among the survivors, the long-term mortality is not impaired. Angiographically, these patients have more severe three-vessel coronary artery disease and incomplete reperfusion of the infarct-related artery.[112] The correlation of site of occlusion to the occurrence of the arrhythmia and the future risk of recurrence of conduction disturbance has not been fully addressed.

Atrial Fibrillation

Atrial fibrillation is a common complication of acute MI, with a reported incidence of 7-18%.[113,114] New-onset atrial fibrillation occurs in about 10% of patients in acute MI in the post-thrombolytic era.[115] Advanced age and the female sex are two universally found associations; the median time from onset of chest pain to atrial fibrillation was two days.[116] Atrial fibrillation is a marker of higher risk baseline clinical and angiographic features. It is associated with larger infarct size (higher peak CPK level), worse Killip class and left ventricular function, increased heart rate, cardiogenic shock, conduction disturbances, ventricular tachycardia and fibrillation, recurrent ischaemia and re-infarction compared with those without the arrhythmia. Angiographically, patients have more extensive (three-vessel) coronary artery disease and RCA involvement, and poorer reperfusion of the infarct-related artery. Moreover, the in-hospital incidence of ischaemic stroke (3.1% versus 1.3%, p=0.0001) was also increased.[115] In-hospital and one-year mortality are invariably worse. Some investigators viewed atrial fibrillation simply as a surrogate of hemodynamic instability. After adjustment of all the possible risk factors affecting the outcome, atrial fibrillation is found to be an independent risk factor of both in-hospital and long-term mortality, even before the onset of the arrhythmia.[116] Anticoagulation is clearly superior to anti-thrombotic therapy for

prevention of stroke and other vascular events (SPAF II, 1994; EAFT, 1993) in atrial fibrillation. The current recommendation for anticoagulation therapy in post-MI patients is either persistent or paroxysmal atrial fibrillation, or left ventricular dysfunction with an extensive regional wall motion abnormality according to ACC/AHA guidelines.[117] In patients with transient, new-onset atrial fibrillation complicating acute MI, the risk of recurrent atrial fibrillation and long-term risk of stroke is unknown. The role of anticoagulation in this patient subset, especially in those with relatively preserved ventricular function, needs further study.

Bundle Branch Block

The presence of bundle branch block in the initial ECG in the setting of acute MI has been reported in decades to have unfavorable short- and long-term clinical outcomes.[118-120] Go, et al.[121] carried out a retrospective analysis of approximately 300,000 acute MI patients. He found that left and right bundle branch block were present in 6.7% and 6.2%, respectively. Patients with bundle branch block are generally older, with more co-morbidity such as diabetes mellitus, peripheral vascular diseases and prior history of Coronary Artery Bypass Graft (CABG).[122] Bundle branch block is found more frequently in anterior wall MI than inferior wall MI.[123] They had larger infarct (higher peak CPK level),[118] lower left ventricular ejection fraction (higher Killip class) and more multi-vessel coronary artery disease, especially LAD involvement.[122] Moreover, they were less likely to receive thrombolytic therapy, aspirin with 24 hours, and beta-blocker.[121] They developed more in-hospital complications like cardiogenic shock, atrio-ventricular block and asystole that required ventricular pacing[124] than those without the conduction disturbance. The unadjusted in-hospital mortality is about twice as high for bundle branch block patients than those without.[121] After multivariate analysis, the adjusted mortality is still significantly higher in bundle branch block patients. Left bundle branch block has been shown to be an independent predictor of in-hospital mortality, rather than right bundle branch block.[122] Conversely, some investigator reported right bundle branch block as the stronger predictor.[121] The increased in mortality rate persists at three years[118] and five years.[125]

Summary

ECG is a simple and indispensable tool in the management of inferior wall MI. It is an essential for diagnosing, and provides an assessment of the size and extent of the infarct, monitor the success of therapy and predict the prognosis. Moreover, careful interpretation of ECG predicts the infarct-related artery and site of occlusion with high accuracy.

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