The Role of Modern Morphologic Electrocardiology in Acute Myocardial Ischemic Syndromes

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The current issue of *IMAJ* features two important prospective studies that assessed the hospital course and 30 day outcome characteristics of patients with acute myocardial infarction. The first study, by Behar et al. [1], stratified the patients with AMI[·] using ST segment deviation, yielding three well-defined groups: a) with ST elevation, b) without ST elevation, and c) with no electrocardiographic changes. The second study, by Amit et al. [2], compared the outcomes of AMI patients treated in a coronary care unit and of those treated in a facility other than a CCU (usually an internal medicine department). I shall try to analyze the current knowledge regarding the interpretation of ST segment deviation in acute syndromes and review its achievements.

ST segment elevation in acute ischemic syndromes

Transient or new persistent ST segment elevation expresses an acute regional transmural ischemia surrounded by healthy myocardium. This regional ischemia is produced by a sudden total obstruction (transient or persistent) of an epicardial coronary artery [3]. Basic electrophysiology has demonstrated that ST elevation recorded by the electrode facing the acute ischemic injury is due to a shortening of phase 2 and 3 of the action potential in the epicardial layer [4].

Molecular biology has provided convincing evidence that epicardial action potential is shortened by an increased level of K^+ in the extracellular space [5]. The abnormal amount of K^+ outside the myocytes is due to an increased amount of adenosine [6]. The adenosine activates the K^+ATP-dependent channels in the ischemic area, inducing hyperpolarization of myocytes and muscle cells of the microcirculation [6]. Thus, the myocytes of the epicardial layer reduce the demand of oxygen, and the microcirculation in the ischemic area reduces the resistance to the coronary flow [6].

It is well known that most infarctions are due to the formation of a red thrombus overlapping a soft atherosclerotic ruptured plaque [7]. All studies on this subject show that patients with ST segment elevation infarction are younger than those without ST depression. Patients with ST elevation infarction are also candidates for thrombolytic and angioplasty reperfusion, as seen in Table 3 in the article by Behar et al. [1].

Non-ST segment elevation in AMI

The vast majority of patients without ST segment elevation are affected by transient or new persistent ST depression There are many types of ST depression with different electrophysiologic mechanisms, hemodynamic consequences, and therapeutic approaches [8–10]. Levine [10] was the first to describe the pre-mortem ECG with severe ST depression in the precordial leads and to compare it with clinical and coronary data and with myocardial pathologic anatomy. He found that the acute infarction involved – in a circumferential way – the entire subendocardium. He discovered a severe mechanical syphilitic or atherosclerotic obstruction of the left main coronary artery in many cases, while in others he found severe three-vessel atherosclerotic disease

Cook and colleagues [11], in a postmortem study, described two types of subendocardial infarction. The first type confirmed Levine's findings: a huge subendocardial infarction with LMCA or severe three-vessel disease, ST segment depression in the precordial leads, and severe cardiogenic pulmonary congestion. The second type was a small subendocardial infarction; but the patient died suddenly and pre-mortem ECG could not be recorded [12].

The experimental laboratory has contributed important data when the LMCA is occluded for a short time in well-instrumented dogs [13]. By occluding the LMCA, the researchers found a shift of pressure/volume relation, up and rightward (an increase in end-diastolic pressure without any increase in the corresponding end-diastolic volume). Grossman's group [14,15] conducted trials with both dogs and humans by increasing the heart rate with atrial pacing overdriving a semi-occluded epicardial artery. Both models showed an increase in left intracavitary end-diastolic pressure without increase in the corresponding end-diastolic volume, accompanied by ST segment depression in the precordial leads.

Thus it may be concluded that an extensive left ventricle ischemia induced by LMCA and an increased heart rate of a semi-obstructed coronary artery exert a common effect on the left

AMI = acute myocardial infarction
CCU = coronary care unit

LMCA = left main coronary artery

ventricle. Both situations induce an increase in end-diastolic pressure and a precordial ST segment depression.

The first hemodynamic effect of ischemia is diastolic dysfunction. It occurs due to the failure of the ATPasa to release Ca from troponin toward the reticulum sarcoplasma. Once the troponin releases the Ca+, the actin myosin breaks up and the myocardium relaxes [16]. Because of the lack of oxygen caused by the reduction of coronary flow, the ATPasa is unable to release energy from the ATP. The failure of this high phosphatase substance results in diastolic dysfunction [17]. In regional myocardial ischemia, the healthy myocardium maintains the intracavitary pressure at normal levels. In circumferential ischemia with ST depression, maximal in V4-V5, or in tachycardia-induced ST depression, severe end-diastolic dysfunction occurs, sometimes causing severe pulmonary edema [8].

An important role is that played by chronic diastolic dysfunction with permanent high diastolic pressure. This clinical situation is found in elderly patients with longstanding hypertension or chronic diabetes [18]. A rapid sinus tachycardia or a rapid atrial fibrillation can induce severe pulmonary edema with a moderate increase in cardiac enzymes, accompanied by ST depression, but with a completely normal coronary tree. These patients are treated in the internal medicine ward, as shown in Tables 1 and 3 of the paper by Amit et al. [2].

In the last decades, experimental and molecular biology has pointed to the important role of the extracellular matrix as a major cause of severe outcome [19]. The increment in the amount of collagen I (steel collagen) causing detriment of collagen III (gel collagen) stiffens the myocardium, thereby inducing diastolic dysfunction and forming the basis for diastolic insufficiency [18]. The contribution of molecular biology enables us to understand that the acute diastolic dysfunction due to an ischemic problem is expressed by a transient ion disturbance. However, the chronic diastolic dysfunction is due to the stiffness of extracellular matrix [19].

Italian researchers used the ergonovine test to confirm the presence of vasoconstriction in patients with acute ischemia and almost normal coronary arteries. They recorded a continuous 12 lead ECG while injecting ergonovine; a maximal ST depression appeared in V2-V4 with a sudden subtotal obstruction of the left descending artery [20]. If the vasoconstriction progresses toward total obstruction of the artery, ST segment elevation appears in the same leads [21]. The Italian group did not have myocardial anatomical data of patients with ST depression in V2-V4, however it is quite logical to assume that it was an induced regional subendocardial ischemia. Angioscopy revealed that in patients with unstable angina, a white thrombus (or thrombocytes) is present that incompletely occludes the lumen of the LAD [22].

In the 1980s a series of clinical investigations were conducted comparing unstable angina with ST segment depression as a result of anginous pain. One of our studies [23] reported the following finding: the ST segment deviation in patients with angina at rest has a different anatomical basis. Almost all patients with ST depression without signs of increased demand during pain at rest are highly predictable to have LMCA, LMCA equivalent, or severe three-vessel disease. We compared the above group with another group having the same clinical parameters, but we recorded ST elevation. In most cases this finding predicted a critical single-artery disease. In a second paper [24] we described the evolving pattern of ST depression and ST elevation toward acute infarction. Patients with ST depression infarction were older, presented severe pulmonary edema, had a high mortality, and the survivors developed non-Q wave infarction. (In patients with unstable angina and ST elevation evolving to acute infarction, the clinical effects are less dramatic, no pulmonary edema is present, the mortality rate is low, and a Q wave infarction develops.) These patients are treated mostly in the CCU, as was shown in both studies published in the current issue [1,2].

Yet another study [25] stressed the clinical, prognostic and coronary anatomy in patients with unstable angina without increased demand recorded during angina at rest. In one group of patients with ST depression, maximal changes were recorded in V4-V5, accompanied by inverted T waves. In most of these patients an obstruction of the LMCA was found. In the other group a maximal ST depression was recorded in V2-V4, but evolving tall and peak T waves. The coronary anatomy was always a subtotal obstruction of the LAD or a total obstruction of the first diagonal artery. In another study we described patients with AMI and isolated ST depression in which maximal changes were recorded in VI-V3. This third group of ST depression recorded in these precordial leads shows the reciprocal early changes of a true posterior wall infarction [25].

The reports by Behar et al. [1] and Amit et al. [2] present important models and a significant database for future studies to advance cardiology and encourage further national research. The ECG early stratification in AMI is crucial for deciding on an emergency therapeutic approach. For patients with AMI and ST elevation there is a well-defined strategy; however, non-ST elevation is a complex problem. ECG re-stratification, in this case, can be helpful to distinguish patients in need of emergency treatment from those who must be "cooled off" in the intensive CCU, or in the non-CCU.

LAD = left ascending artery

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Dancing is a perpendicular expression of a horizontal desire

George Bernard Shaw (1856-1950), Irish playwright and critic. An active member of the Fabian Society he combined a passion for social reform with fierce wit in his numerous writings.

Capsule

A giant virus in amoebae

During a study following a pneumonia outbreak in 1992, a microorganism growing in amoebae and resembling a small gram-positive coccus was isolated from the water of a cooling tower in Bradford, England. Despite attempts with various extraction protocols and low-stringency polymerase chain reaction, no amplification product was obtained with universal 16S rDNA bacterial primers. In their study of this microorganism within Acanthamoeba polyphaga, Scola and colleagues revealed a characteristic viral morphology with mature particles of 400 nm in diameter and surrounded by an icosahedral capsid. This structure is consistent with the finding that Mimivirus is not filterable through 0.2 m pore size filters. No envelope was observed, but 80 nm fibrils attached to the capsid were visible. A typical virus developmental cycle, including an eclipse phase, was observed. As it resembles a bacterium on gram staining, it was named Mimivirus (for Mimicking microbe). Mimivirus has a double-stranded DNA circular genome of about 800 kilobase pairs (kbp). Its genome is thus larger than the sequenced genomes of several bacteria, including *Mycoplasma genitalium* (580 kbp). Mimivirus is a nucleocytoplasmic large DNA virus (NCLDV). This group of viruses includes four other families, including the enveloped Poxviridae, which infect vertebrates (Chordopoxvirinae) and insects (Entomopoxvirinae). The three others are also icosahedral. Iridoviridae and Phycodnaviridae are aquatic viruses, and Asfarviridae infect vertebrates. Whole genome shotgun sequencing is underway.

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