Editorial Comment

Ischemia at a Distance—So Close Yet So Far*

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ST segment elevation in characteristic electrocardiographic leads during an acute myocardial infarction generally allows correct identification of the coronary artery occluded (1). Electrocardiographic changes, usually ST segment depression, are often noted in other leads, presumably representing myocardium subserved by other coronary arteries. What do such changes mean? Are they a benign electrical phenomenon or a harbinger of trouble ahead?

Ekmecki et al. (2) noted that ST segment elevation recorded directly from the anterior epicardial surface after left anterior descending coronary artery ligation in the dog was immediately associated with ST segment depression recorded from the epicardial surface of the posterior left ventricular wall, directly opposite the evolving infarct (Fig. 1). Approximately 15 to 20 minutes later, electrodes from the periphery of the infarct, initially recording mild ST elevation, began recording ST depression as well, with the surrounding normal tissue demonstrating isoelectric ST segments. Hence, ST depression was not only a secondary electrical phenomenon, as evidenced over the posterior wall opposite the infarct, but also a marker of injury or infarction, most likely subendocardial in location, at the margins of the infarct. Nonetheless, the concept that ST depression represented only a secondary or "reciprocal change" in the presence of an acute myocardial infarction became firmly entrenched in electrocardiographic parlance.

Review of hypotheses based on previous clinical studies. Recently there has been renewed interest in the significance of ST segment depression in electrocardiographic leads presumably remote from the zone of the acute infarction. Schuster and Bulkley (3) noted multivessel coronary disease in 20 autopsy patients with postinfarction chest pain associated with electrocardiographic changes (usually ST depression), recorded in leads remote from the zone of the occluded vessel. They coined the phrase "ischemia at a distance" and subsequently noted that in 72 patients with early postinfarction angina, the 43 with "ischemia at a distance" had a mortality rate of 72% by 6 months after infarction, with death often sudden due to ventricular arrhythmia (4). At autopsy, the findings were similar to their earlier autopsy series: small infarcts, in general, in the presence of severe multivessel disease. Thus, mortality appeared to be related to recurrent ischemia, as opposed to a large primary infarction.

Shah et al. (5,6) noted that among patients who presented to the coronary care unit with acute inferior myocardial infarction, those with ST segment depression in the anterior precordial electrocardiographic leads had a lower ejection fraction associated with more severe wall motion abnormalities (as determined by radionuclide ventriculography a mean of 16 hours after infarction), a much greater incidence of left ventricular failure and a higher in-hospital mortality rate (general due to pump failure) than did patients without anterior ST depression. Salcedo et al. (7) reported that ST depression in the anterior leads in patients with acute inferior infarction was highly predictive of a complicated course associated with postinfarction angina, pump failure or recurrent ventricular arrhythmias. Of 24 patients with ST depression in anterior leads, 23 were subsequently found at angiography or autopsy to have severe disease of the left anterior descending coronary artery. Goldberg et al. (8), using radionuclide measurement of regional left ventricular function in patients a mean of 22 hours after acute inferior infarction associated with anterior ST depression, showed that 13 of 14 patients had both inferior and posterolateral wall dysfunction and had a lower global ejection fraction compared with those without anterior ST changes. These investigators suggested that infarction in the distribution of a right coronary artery supplying a portion of the posterolateral ventricle could have produced these wall motion abnormalities without invoking multivessel disease. Other studies have also demonstrated that anterior ST depression during an acute inferior infarction was correlated with a lower rest ejection fraction (9,10), coexisting multivessel disease (10–12) and a more complicated immediate (9,10,13) and long-term (9,10,12,13) clinical course due to a large primary infarction or recurrent ischemia in the presence of multivessel disease.

Despite these clinical studies, at least three published studies reported no clinical, angiographic or hemodynamic differences in patients with acute inferior infarction with or without anterior ST segment depression (14–16) or acute anterior infarction with or without inferior ST depression (16). However, these studies were performed early (mean 4.7 to 7.3 hours) after infarction, and immediately preceded an infarct-sparing or thrombolytic intervention that might have obviated a larger infarct or more complicated postinfarction course after the earliest hours. The Aspirin Myo-

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They concluded that ST depression in the remote zone did not represent an incidental electrical phenomenon related to the vantage point of the electrode, but reflected a large mass of myocardium at risk for infarction without multivessel disease. Their argument would have been supported by angiographic or radionuclide assessment of ejection fraction and regional wall motion in patients with and without ST segment depression in remote zones.

**Clinical implications.** Thus, from experimental and clinical studies, we now know that ST segment depression in remote leads during an acute myocardial infarction may reflect 1) widespread ischemia due to a coronary artery with a larger than usual region of perfusion, 2) ischemia due to multivessel disease, or 3) a benign electrical phenomenon. Unfortunately, it does not appear feasible to know which of these three possibilities is occurring in a patient in the earliest hour or hours after acute myocardial infarction. I believe that the weight of clinical evidence suggests that patients with acute inferior infarction with remote significant ST depression are at somewhat higher risk for serious hemodynamic and clinical sequelae. There is too little clinical information on anterior myocardial infarction (which tends to be large) and inferior ST depression to draw similar conclusions. The multicenter thrombolysis trial (TIMI) may allow resolution of the controversy. However, from the point of view of probability, patients with recurrent chest pain and ST segment changes in remote leads in the hours to days after acute myocardial infarction are most likely experiencing ischemia related to severe multivessel disease. Such patients are at high risk and deserve prompt evaluation and consideration for therapy to improve blood flow to persistently ischemic myocardium.

**References**


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