Editorial

Patients with suspected myocardial infarction presenting with ST segment depression

Acute myocardial infarction in association with predominant ST segment depression on the electrocardiogram is accompanied by high mortality that appears to be little influenced by thrombolytic therapy.[1–3] Patients with ST segment depression have less myocardial damage but a poorer outcome than those with initial ST segment elevation.[3 4]

Clinical characteristics, ECG data, and prognosis

ST segment depression of $\geqslant$ 3 mm is highly specific for diagnosis of acute myocardial infarction. Patients with this finding are generally older and have a history of previous infarction. Most have severe coronary artery disease.[5] Their one and three year outcomes are poorer than those of other infarct patients including those with initial ST segment elevation.[4 6] The majority of deaths occurs within one week of presentation.[7]

Patients with non-Q wave infarction can present with either ST segment elevation or depression on their admission ECG.[8–10] Those with ST depression have a higher rate of pump failure, multivessel disease, and mortality than those with ST elevation (including those with concomitant ST depression) or isolated T wave changes.[8] Despite a smaller infarct, the ST depression patients have a lower left ventricular ejection fraction, more in-hospital complications, and a higher incidence of previous myocardial infarction.[9] In patients with non-Q wave infarction who survived for at least one year after recruitment into the Diltiazem Reinfarction Study,[10] the mortality was highest in the subgroup with persistent ST depression. Furthermore, persistent ST depression was the highest independent predictor of mortality, being more discriminating even than old age or a history of heart failure.

Pathophysiology

In a postmortem study of patients with transmural and subendocardial infarctions, Raunio *et al*[11] showed that the majority of patients with subendocardial infarction had had ST depression rather than ST elevation in their presenting ECG, and many had evidence of previous infarction. Interestingly, some patients with transmural infarction had only ST depression in the ECG.

It is likely that ST depression without elevation might be caused by the cancelling out of electrical events caused by infarction in opposite myocardial planes. Thus a new anterolateral infarct could normalise the ECG changes of a previous healed inferior infarct by subtracting anterior and lateral dipole contributions from the QRS complex, resulting in ST segment and/or T wave changes as the sole ECG change. Patients with severe ST depression seem likely to fall within this category.

Thrombolytic therapy

In patients with suspected myocardial infarction who presented with ST depression in the GISSI trial,[2] hospital mortality was slightly though not significantly higher in those who received streptokinase than among those who did not. The ISIS-2 trial[1] and the meta-analysis from the Fibrinolytic Therapy Trialists,[3] which included 3563 patients presenting with ST depression, confirmed the apparent lack of thrombolytic efficacy. A small Auckland study[12] randomised patients presenting within six hours of chest pain with $\geqslant$ 1 mm ST segment depression to receive streptokinase or placebo and observed no difference in mortality, reinfarction or number of revascularisation procedures at one year. The LATE study[13] compared the effect of tissue plasminogen activator (tPA) or placebo in patients who presented six to 24 hours after onset of chest pain. There was a significant reduction of one year mortality in the tPA group of 528 patients with confirmed infarction and $\geqslant$ 2 mm ST segment depression compared with placebo patients.

Several possible explanations might account for the apparent inefficacy of thrombolytic therapy. First, the ISIS-2,[1] GISSI,[2] and the small Auckland study[12] included patients with < 3 mm of ST segment depression, many of whom are likely to have unstable angina rather than infarction. Thrombolytic therapy is ineffective in unstable angina, therefore, their inclusion would have diluted any possible benefit for those with infarction. Second, as many patients will have had previous infarction, even limited necrosis might result in critical left ventricular damage. Logically, however, such patients should still benefit from thrombolysis if given sufficiently early to limit the extent of myocardial necrosis. Third, patients may have more extensive and severe underlying coronary disease so that even with thrombolysis, coronary blood flow might be inadequate to salvage myocardium; previous studies have shown that only TIMI (Thrombolysis in Myocardial Infarction) grade 3 (normal flow) is associated with an improved outcome. Finally, unlike the rapidly developing thrombus that follows acute plaque rupture, the thrombus might develop at the site of critical stenosis, resulting in extensive fibrin cross links or be rich in platelets and subsequently be resistant to thrombolysis.

Antiplatelet treatment

In the ISIS-II trial,[1] aspirin treatment was associated with a non-significant reduction in mortality in patients with ST depression. In the RISC study,[14] aspirin significantly reduced the rate of myocardial infarction and death in patients with non-Q wave infarction, many of whom had presented with ST depression. Monoclonal antiplatelet GPIIb/IIIa antibody in combination with thrombolytic

therapy was effective in achieving sustained coronary arterial recanalisation in canine models and offers promise. Trials are currently in progress to assess the efficacy of potent antiplatelet agent in treating patients with acute ischaemic syndrome.

Heparin treatment

In a meta-analysis, the addition of heparin to aspirin significantly reduced risk of myocardial infarction and mortality in patients with unstable angina and non-Q wave infarction.[15] The RISC study[14] randomised patients with unstable angina or non-Q wave myocardial infarction (many of whom had ST segment depression) to aspirin, heparin or placebo. Patients given a combination of aspirin and heparin had the lowest rate of myocardial infarction or death in the initial five days. The ATACS trial[16] on similar patients showed aspirin with heparin followed by warfarin to be superior to aspirin alone in reducing recurrent ischaemic events. Importantly, in patients with non-Q wave infarction, most of the reinfarctions or deaths occurred within one week of randomisation.

Angiotensin converting enzyme inhibitors and β blockers

Many of the patients presenting with ST depression will have had previous infarcts; therefore, the use of angiotensin converting enzyme inhibitors and β blockers, both of which have been shown to be beneficial in high risk patients with impaired left ventricular function, is logical and should be considered.

Future research and management of patients with ST depression

It is logical to anticipate that early reperfusion will improve outcome and we believe that this is the only therapy that offers a realistic prospect of reducing the high mortality in patients with ST depression. In patients with $\geqslant$ 3 mm ST segment depression, aspirin and antiangina treatment such as buccal nitrates should be administered and the ECG repeated 15 minutes later. If the ST segment depression persists or worsens the patient is likely to be infarcting. For these patients, primary angioplasty or coronary bypass surgery might be the best option. However, if such an interventional approach is not feasible, administration of a rapidly acting thrombolytic agent should be considered. Heparin should be given if thrombolysis is contraindicated. As most reinfarctions or deaths occur within the first few days of presentation, coronary angiography and revascularisation procedures, if appropriate, must be performed early. β blockers and angiotensin converting enzyme inhibitor should be used if there is evidence of heart failure or poor left ventricular function. Future research should focus on the effect of thrombolysis, the newer antiplatelet agents, and coronary revascularisation alone or in combination.

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