Early thrombolytic therapy in acute myocardial infarction has for years been shown to reduce cardiac mortality and morbidity[1]. Large multicentre trials have established that the beneficial effect of thrombolysis is inversely correlated to the time delay from onset of chest pain to the start of reperfusion therapy[2]. The decline in treatment efficacy is steepest in the first hours after symptom onset[2,3].

In this issue, Wong et al.[4] address the value of non-invasive prediction of myocardial salvage following thrombotic therapy. A modified QRS score from the admission standard static 12-lead electrocardiogram (ECG) and conventional QRS scoring from the discharge ECG were used to calculate myocardial salvage, and a mean of 50% salvage after thrombolysis was found. The beneficial effect of thrombolytic therapy was inversely correlated to the Selvester QRS score found on the admission ECG, to the initial Q-wave grade, and to the T-wave inversion grade. TIMI flow grade at 90 min, the number of leads with ST-segment depression, and the maximum size of ST-segment depression were positively correlated to myocardial salvage. In multivariate analysis, a high QRS score or the presence of T-wave inversion on the admission ECG were predictors of low myocardial salvage. It was also noted that there was no correlation between myocardial salvage and time from symptom onset to start of thrombolytic treatment.

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Is time the overriding factor in thrombolytic therapy?

See page 399, doi:10.1053/euhj.2001.2795 for the article to which this Editorial refers


Non-invasive methods to estimate the effects of reperfusion therapy using thrombolytic medication have been validated for around 15 years, and, based on the literature available, the methods used appear to be reliable predictors of clinical outcome. The most frequent non-invasive method of assessing coronary reperfusion was by estimating total ST-segment elevation in all leads of the ECG, except for aVR, taken on admission and again at 90 to 180 min after the start of thrombolytic therapy. Finally, the ST-segment recovery rates were calculated[5]. It has been clearly shown that ST-segment recovery is positively correlated to the size of the left ventricular ejection fraction[6] and an improved short- and long-term prognosis[7]. On the basis of the consistent findings in the literature, measurements of ST-segment recovery have been adopted in numerous clinical studies, and the changes in the ECG seem to be a reliable surrogate end-point with which to assess the effects of thrombolytic therapy.

Another non-invasive method of quantifying the effects of thrombolytic treatment is to calculate myocardial salvage. This can be done by estimating the final infarction size from the discharge ECG by use of the Selvester QRS scoring system[8], combined with assessment of myocardium at risk, judged from the ECG at the time of admission. Formulas describing different characteristics of ST-segment elevation are used for this. Ultimately, the ratio between the two ECG measurements can be calculated. By appropriate use of this method, a positive correlation between myocardial salvage and left ventricular systolic function, together with TIMI flow grade after thrombolysis, have been reported[6].

The estimation of jeopardized myocardium in the study by Wong et al[9] was made using a modified version of the QRS scoring system. The method was originally described in 1996 by Juergens et al[10], who, in 28 patients with a first acute myocardial infarction, demonstrated a close relationship between the QRS score on the admission ECG and the myocardium at risk judged from perfusion defects on a Thallium (Tl)-201 scintigraphy performed prior to thrombolytic therapy. The results presented in this issue[4] are thus based on a quantitatively flimsy methodological foundation and further validation of the modified QRS scoring system is warranted in order to put the method in an appropriate scientific and clinical perspective.

Nevertheless, there are two major points of interest in the study by Wong et al[11]. Firstly, the observation that myocardial salvage is inversely correlated to the initial QRS score and T-wave inversion grade on the presenting ECG, and secondly the finding that myocardial salvage did not correlate with time from onset of chest pain to the beginning of thrombolytic treatment. The first message is consistent with what is to be expected: the more Q waves and negative T waves on the electrocardiogram at hospital admission, the more myocardial necrosis and consequently the less potentially salvageable myocardium.

The second message, however, is more controversial, as we have all been taught that from a prognostic point of view the time frame from symptom onset to the start of reperfusion therapy is crucial. How do we fit in the observations by Wong et al.? One theory could be that as long as Q waves have not developed, there still may be a role for thrombolytic therapy, even if the time frame of 12 h from onset of symptoms has passed. It should be acknowledged that patients’ recollection of the duration of chest pain may be imprecise and does not necessarily correlate with the progression of myocardial necrosis. Also the presence of prodromal angina before the acute myocardial infarction may be a confounder in the assessment of the duration of chest pain as perceived by the patient. Finally it is well established that approximately 25% of myocardial infarctions are clinically silent[12].

In most cases the presence of Q waves will reflect irreversible myocardial damage, and if such changes have developed at hospital admission, the potential benefit from thrombolysis may be absent, even if the time delay is less than 3–6 h. However, in the LATE study[11], the decision to start thrombolytic treatment was taken 6–24 h after onset of chest pain. Thus, in this large scale trial, patients who had insufficient ECG evidence for therapy on admission could still be included, if such evidence became available later. Subgroup analysis suggested that some patients may have had an improved prognosis, even when reperfusion treatment was initiated after 12 h[11].

The present study only included 146 patients, and because of the complexity of the reperfusion process, several other factors besides the time span from onset of chest pain to start of thrombolysis will interact and may serve as confounders in the interpretation of the importance of the time window. Thus, the occurrence of functional neutralizing antistreptokinase antibodies arising as a result of streptococcal infections have been demonstrated[12]. Furthermore, there may be abnormalities in the plasminogen molecule resulting in an imperfect conversion to plasmin or inability to complex with streptokinase. Moreover, congenital or acquired plasminogen deficiency will probably influence the results[13]. A severe underlying, fixed stenosis may be present in the involved coronary artery, and even after successful thrombolysis, the coronary stenosis may cause impaired myocardial
perfusion. Additionally, thrombolysis can result in peripheral embolization with subsequent compromised myocardial perfusion. Treatment with streptokinase and heparin might result in increased thrombogenesis with possible reocclusion due to formation of thrombin and activation of platelets.\(^{[14]}\)

To date, the issue whether or not the presence of pathologic Q waves in the admission ECG of patients with acute myocardial infarction should be decisive in giving thrombolytic therapy has not been clarified. Should we ignore the time frame given by the patient when Q waves are absent? Should we extend the time window for reperfusion therapy in such cases? The study by Wong \textit{et al.}\(^{[4]}\) contributes significantly to this important issue, but it should be emphasized — as stated by the authors themselves — that the results are only applicable to patients with a first acute myocardial infarction. Larger studies addressing the relative clinical importance of the time window vs QRS score in thrombolytic therapy are warranted.

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Vulnerable plaques: let’s stop sinking on submerged icebergs?

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Advanced percutaneous coronary interventions have dramatically changed our approach to patients with overt coronary artery disease, from prompt recanalization of the occluded artery in acute myocardial infarction to multivessel treatment of complex lesions with stents. Radiation therapy and drug-eluting stents hold the promise of controlling hyperplasia after treatment and of obtaining long-term patency of stenotic or occluded segments. However, the efficacy of interventional cardiology to prevent the myocardial damage induced by coronary atherosclerosis has...