The unresolved mystery of stress-induced ST segment elevation after myocardial infarction

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Studies of the relationship among stress-induced ST segment elevation, myocardial viability and ischaemia after myocardial infarction have gained increasing interest, particularly in the thrombolytic era, as a large proportion of patients retain viable myocardium which may improve spontaneously or after revascularization[1–4]. It is important to identify viable myocardium in order to match patients to the most appropriate strategy for improvement of left ventricular function.

In this issue, Mezilis et al. studied the value of dobutamine- and exercise-induced ST segment elevation shortly after acute myocardial infarction in the prediction of improvement of regional and global left ventricular function after revascularization in 39 patients[5]. They concluded that there is a strong association between dobutamine- and exercise-induced ST segment elevation and functional recovery following revascularization. Exercise-induced ST segment elevation in more than three leads, the development of ST segment elevation in both tests and a biphasic response during dobutamine echocardiography accurately predicted functional recovery. This study confirms the value of electrocardiographic studies during stress testing and shows that a simple method with little interpretation bias can be as useful as sophisticated methods in the detection of myocardial viability. The relationship between dobutamine-induced ST-segment elevation and late functional recovery after acute myocardial infarction is consistent with our previous report as well as those of other investigators[1,2,4].

One of the limitations of this study is the exclusion of patients with severe left ventricular dysfunction, as studies of myocardial viability are most useful in such patients.

Relationship between ST segment elevation and myocardial ischaemia

Many studies have concluded that stress-induced ST segment elevation is not a specific sign of regional myocardial ischaemia after myocardial infarction as opposed to patients without previous infarction[1,3,6]. Most of these studies demonstrated a similar prevalence of ischaemia in patients with and without ST segment elevation. It is difficult to explain the apparent contradiction between the positive relationship with myocardial viability and the lack of correlation with regional ischaemia. One of the possible explanations is that ST segment elevation may be related to myocardial stunning rather than myocardial hibernation. In fact, most of the studies that demonstrated a higher prevalence of viability in patients with ST segment elevation were conducted after acute myocardial infarction[1,2,4,5]. In these patients, late spontaneous recovery of function may occur consistent with myocardial stunning as the major mechanism of reversible dysfunction. The absence of regional ischaemia in this case is in favour of spontaneous recovery of function as ischaemia may interfere with functional improvement or induce myocardial hibernation. However, in the study of Mezilis et al.[5], ST segment elevation was associated with a higher prevalence of a biphasic response, which is presumably a sign of myocardial ischaemia. It is not clear from this paper how many patients developed ischaemia in normally contracting myocardium at rest in the distribution of the infarct-related artery. The possibility that late functional recovery was due to spontaneous changes of myocardial perfusion and function rather than revascularization in some patients cannot be excluded[7].

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Patients with old myocardial infarction

Studies of the relationship between ST segment elevation and myocardial viability in patients with chronic left ventricular dysfunction are scarce\[^8,9\]. The relationship between ST segment elevation and myocardial viability is apparently dependent on the patient’s characteristics, particularly the likelihood of having inducible ischaemia and the time elapsed after myocardial infarction. Patients studied after a recent myocardial infarction are usually screened for functional evaluation before discharge and therefore, the prevalence of ischaemia is not high; meanwhile the prevalence of myocardial stunning is high as compared to symptomatic patients with chronic left ventricular dysfunction late after myocardial infarction. There is evidence from studies that myocardial ischaemia, viability and the presence of myocardial aneurysm may independently underline stress-induced ST segment elevation after myocardial infarction. The different conclusions of previous studies regarding the functional significance of ST segment elevation may be explained by the variable prevalence of myocardial viability and ischaemia in the peri-infarction zone among different patient populations. We have recently demonstrated that the significance of ST segment elevation is different in predominantly asymptomatic patients with recent infarction, compared to symptomatic patients with old infarction referred for revascularization. In the former group, ST segment elevation was associated with a higher prevalence and extent of late improvement of function — mostly without revascularization\[^1\], consistent with the findings of Mezlis et al.\[^5\] and Piérard et al.\[^2\]. However, in symptomatic patients with chronic left ventricular dysfunction, we demonstrated that ST segment elevation was not associated with a higher prevalence or extent of improvement of function after revascularization\[^9\]. In that study, dobutamine-induced ST segment elevation occurred in the majority of patients with Q wave myocardial infarction referred to CABG of the infarct-related artery. The prevalence of regional ischaemia was high (83%) but comparable to patients without ST segment elevation, reflecting the high pre-test likelihood of inducible ischaemia in symptomatic patients referred for CABG. Most patients (80%) with dobutamine-induced ST segment elevation pre-operatively had little or no ST segment elevation after CABG. The lack of re-induction or a reduced level and extent of dobutamine-induced ST segment elevation after CABG correlated with absent re-induction of regional ischaemia in 93% of patients with pre-operative ischaemia. Other functional changes were resection of scarred myocardial seg-

ments in 20% and improvement of baseline regional function in 25% of patients. In 50% of patients the only underlying functional change associated with absent or lower level of dobutamine-induced ST segment elevation after CABG was lack of re-induction of regional ischaemia. Re-induction of ST segment elevation with dobutamine after CABG correlated with worsening of regional function or re-induction of regional ischaemia in most patients. Fox et al.\[^8\] reported that in 19 patients with Q wave myocardial infarction and exercise-induced ST segment elevation, CABG resulted in abolition of ST segment elevation in 11 with symptomatic improvement and sustained graft patency and no change of left ventricular function. This shows that the relationship between myocardial ischaemia and ST segment elevation in Q waves is causal rather than coincidental in a significant proportion of symptomatic patients with old myocardial infarction, despite the possible contribution of other factors, such as myocardial viability or myocardial aneurysm in some patients.

Ischaemia in non-infarcted myocardium

ST segment elevation may be associated with peri-infarction ischaemia in the absence of myocardial viability. This scenario is likely to occur when ischaemia involves myocardial regions with normal resting function adjacent to a necrotic myocardium in the distribution of the infarct-related artery. Animal studies have shown that acute ischaemia adjacent to a chronic infarction induces ST segment elevation at the surface of the scar despite the virtual absence of viable tissue within the infarction, suggesting a passive ST segment potential transmission through the infarction\[^60\]. In this case, revascularization may not result in an improvement of left ventricular function. In contrast, patients with recent myocardial infarction may develop ST segment elevation due to the presence of stunned myocardium that improves spontaneously in the absence of regional ischaemia. Therefore the pathophysiological significance of dobutamine-induced ST segment elevation may differ between patients with recent and old myocardial infarction. In the former group, the prevalence of myocardial viability is high compared to patients with old infarction. It has been shown that the majority of recently infarcted myocardial regions retain residual metabolic activity, the extent of which is inversely related to the time elapsed from the occurrence of the acute event\[^1\]. On the other hand, symptomatic patients with old infarction may have more inducible
ischaemia and less myocardial viability and therefore, ST segment elevation in this group is related more to myocardial ischaemia and occasionally myocardial aneurysm.

From these data, it may be concluded that any sort of heterogeneity of myocardial contraction in the infarct zone may be responsible for stress-induced ST segment elevation. This may represent myocardial viability, in which case a viable segment improves function relative to an adjacent necrotic segment or peri-infarction ischaemia. Thus, a myocardial segment in the infarct region demonstrates worsening of function relative to a normal or necrotic adjacent region. This mechanism is more complex in the setting of myocardial hibernation. Here viable segments are supposed to improve at low dose dobutamine (or low grade exercise) and worsen at higher stress levels, consistent with the biphasic response. However, in the presence of severe ischaemia, the contractile response of viable myocardium to low dose dobutamine may be blunted.

**Future directions**

Many questions remain to be answered for the further clarification of the significance of stress-induced ST segment elevation after myocardial infarction.

1. Is there a relationship between the time onset of ST segment elevation during stress and its functional significance?
2. Does improvement of function or amelioration of myocardial ischaemia have an impact on late re-induction of ST segment elevation?
3. What is the prognostic value of stress-induced ST segment elevation and how may it differ between patients with and without revascularization?
4. Can the results of this study be extrapolated to patients with more severe left ventricular dysfunction who represent the target population for viability studies? Further studies will be needed to establish the value of stress-induced ST segment elevation in the risk stratification and the selection of management strategies after myocardial infarction.