prognosis and that, equally important, the beneficial effect of thrombolytic therapy is not influenced by the smoking status of the patient. The relevance of these findings for daily cardiological practice may be modest because, quite rightly, acute treatment decisions should not be based on the smoking status of the patient presenting with an acute coronary syndrome. On the other hand, the smoker’s paradox has been rebutted by the Greek study and the prognosis of the smoker with an acute coronary event now seems clearer and less of a paradox than previously. While it is unlikely that these findings will receive much attention outside the medical community, the data enable us, at least, to deliver a clear and straightforward message to all smokers, whether they are patients or still healthy. That is, in my opinion, the most welcome contribution from the Greek study.

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Ventricular function after primary angioplasty for acute myocardial infarction: correlates and caveats

See page 785 for the article to which this Editorial refers

Reperfusion therapy is by far the most important therapy administered to patients suffering acute myocardial infarction. Of the three forms of reperfusion therapy currently available — primary angioplasty, thrombolytic therapy, and coronary bypass surgery — primary angioplasty is the most efficacious, when it can be administered rapidly and expertly[4]. The lower mortality associated with primary angioplasty is believed to be due to its ability to achieve reperfusion more rapidly in a greater number of patients than the other forms of reperfusion therapy[2]. Primary angioplasty is also associated with an approximately 50% lower risk of reoclusion than thrombolytic therapy (and still lower if stents are used)[3]. It has been hypothesized that there may be benefits from the greater patency rate associated with angioplasty independent of myocardial salvage, such as reducing unfavourable late remodelling, greater electrical stability, and the ability to provide collaterals to coronary occlusions that may develop in the future[4]. However, the ability to achieve more rapid reperfusion in a greater number of patients is believed to be the primary explanation for the lower mortality associated with primary angioplasty. More timely reperfusion, particularly when it is within 6 h of
symptom onset, leads to greater limitation of infarct size and preservation of myocardial infarction. Ventricular function may be impaired for days to weeks following achievement of even complete reperfusion, due to a phenomenon that has been termed ‘myocardial stunning’ — profound metabolic derangement due to prolonged ischaemia that impairs ventricular systolic and diastolic performance, but is insufficient to cause cell death[5]. Therefore, assessment of ventricular function after reperfusion therapy for acute myocardial infarction should be performed 2 months after infarction to detect late improvement in ventricular function, should myocardial stunning have occurred.

Despite the greater reperfusion rate associated with primary angioplasty, measurements of left ventricular function among patients enrolled in trials comparing primary angioplasty and thrombolytic therapy have not always revealed a difference in left ventricular ejection fraction among patients treated with primary angioplasty and lytics. However, ventricular function is a difficult end-point to assess when comparing two therapies if one has a lower mortality than the other[6]. More critically ill patients in the group who receive the therapy with the lower mortality (primary angioplasty) will survive to have their reduced ventricular function assessed than in the group receiving the less effective therapy (thrombolytic therapy). Therefore, the mean left ventricular ejection fraction in the two groups might be similar when, in reality, greater limitation of infarct size and preservation of ventricular function is the basis for the improved survival with the more effective therapy.

In this issue, Ottervanger and others report on the recovery of left ventricular function in the 6 months after primary angioplasty for acute myocardial infarction[7]. This talented group of investigators has performed several studies confirming the superiority of primary angioplasty over thrombolytic therapy. Their current study provides additional supportive data. Over 4 years, they treated 785 patients with primary angioplasty; the 6-month mortality in this unselected group of patients was only 5%. Only 3% had a recurrent non-fatal infarction during the 6-month follow-up period. In this study, Ottervanger et al. analysed 600 of these patients with paired ejection fractions measured by radionuclide ventriculography on the 4th day and 6 months after infarction. They report a 3% improvement in mean ejection fractions among these patients. Independent predictors of recovery of left ventricular function included anterior site of infarction, single vessel coronary disease, and a more severely depressed ejection fraction at baseline. Surprisingly, time to treatment was not an independent predictor.

A number of points are worth mentioning. The observation that patients with the lowest ejection fractions had the greatest increase in ejection fraction is in part a reflection of regression to the mean. Regression to the mean describes the phenomenon that repeat measurements of ventricular function are most likely to appear to ‘change’, even if no real change has occurred, when they lie at the extremes of measured results, due solely to variability in measurement. Also, patients with the lowest ejection fractions in whom improvement in ventricular function does not occur are more likely to die and be excluded from analysis since they will not have a second ventriculogram to analyse, which may also contribute to the finding that patients with the lowest initial ejection fractions have the greatest increase in ventricular function. In addition, the lack of an association between time to treatment and rise in ejection fraction is counterintuitive. Several studies have revealed an important relationship between time to treatment with direct angioplasty and mortality, as has been conclusively demonstrated with thrombolytic therapy[8,9]. It is likely that the slope of the relationship between treatment and mortality differs between direct angioplasty and thrombolytic therapy. Later treatment with thrombolytic therapy is less effective — that is, associated with a lower reperfusion rate — because of changes in the composition of the coronary thrombus with time; in addition, later treatment has also been associated with an increase in the risk of myocardial rupture[10,11]. There are also data indicating that haemorrhagic stroke is more frequent when thrombolytic therapy is administered late[12]. In contrast, direct angioplasty is as likely to be successful late in infarction as it is early after symptom onset, and an increase in myocardial rupture with late angioplasty has not been reported[13]. However, there can be little doubt that earlier treatment with angioplasty leads to greater limitation of infarct size and preservation of myocardium, and affords patients the greatest opportunity for late improvement in ventricular function. In the analysis by Ottervanger et al.[7], patients with an ischaemic time of less than 6 h were compared to those with an ischaemic time of greater than 6 h, and a trend toward a greater increase in LVEF in patients with an ischaemic time of less than 6 h was present (6·1% vs 5·2%, respectively, \(P = \text{ns}\)). It would have been more appropriate if time to treatment and a rise in ejection fraction had been measured as continuous variables in a regression analysis, which would increase the power to detect a relationship between times of treatment and recovery of ventricular function. Analysed as it was in this study, there was limited power to detect a relationship between time to
treatment and recovery of ventricular systolic function, and there is nothing in this study that negates the belief that ‘time is muscle’, and that the earlier reperfusion is performed, the better the outcome.

Nonetheless, these investigators are to be congratulated for this study which, along with their many prior studies, have helped identify why and to what extent primary angioplasty is the most effective form of reperfusion therapy for patients suffering acute myocardial infarction.

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