Assessment of myocardial viability: guide to prognosis and clinical management

See page 981 for the article to which this Editorial refers

Over the past two decades it has become clear that depressed left ventricular function in patients with chronic coronary artery disease is not necessarily an irreversible process, but that improvement of left ventricular function following revascularization may be anticipated in patients with dysfunctional but viable myocardium. Numerous studies employing a variety of techniques have demonstrated that the majority of the dysfunctional but viable segments improved in function following adequate revascularization.

Currently, four techniques are predominantly used for the identification of viable myocardium, each based on a different ‘hallmark’ of viable tissue (Table 1). These different characteristics include (1) preserved glucose utilization, (2) cell membrane integrity, (3) intact mitochondria, and (4) preserved contractile reserve. The first three characteristics are usually evaluated by scintigraphic techniques: fluorine-18-fluorodeoxyglucose traces glucose utilization, thallium-201 uptake reflects cell membrane integrity, and technetium-99m sestamibi (or tetrofosmin) uptake corresponds (at least in part) to intact mitochondria. The fourth characteristic, i.e. preserved contractile reserve, can be probed by echoangiography using dobutamine stress. Alternatively, dobutamine stress using magnetic resonance imaging has been put forward as an accurate measure for assessing myocardial ischaemia and viability. All these imaging techniques have reported high accuracies to predict improvement of regional left ventricular function following revascularization (Fig. 1). Advantages of the nuclear imaging modalities and magnetic resonance imaging over dobutamine stress echocardiography is the option of quantitative, operator-independent analysis of the former, as compared to the visual, operator-dependent analysis of the latter. Moreover, transthoracic dobutamine stress echocardiography is not feasible in a substantial number of patients (varying from 15% to 40%) due to an inadequate acoustic window.

In the current paper by Baer et al., the authors have proposed two possible alternative approaches to overcome the latter of the two shortcomings of transthoracic echocardiography: dobutamine transesophageal echocardiography and dobutamine magnetic resonance imaging. They convincingly showed that dobutamine transesophageal echocardiography and dobutamine magnetic resonance imaging were feasible in 97% and 98% of the patients, respectively. Moreover, both approaches yielded comparable accuracies for the prediction of improvement of regional left ventricular function following revascularization, as compared to the other techniques (Fig. 1). Assessment of contractile reserve by quantitative analysis was not addressed, as both the dobutamine magnetic resonance imaging and the dobutamine transesophageal echocardiography data were analysed visually. In particular, dobutamine magnetic resonance imaging is very well suited for quantitative analysis. In a previous work from the authors, however, it was shown that dobutamine magnetic resonance imaging, when analysed quantitatively, yielded only slightly higher sensitivities and specificities for the prediction of improvement of function as compared to the results in the current, visual analysis. However, it would be of interest to perform a head-to-head comparison between quantitative and visual analysis using either dobutamine magnetic resonance imaging or dobutamine transesophageal echocardiography.

Besides the end-points used in the study by Baer et al., i.e. recovery of regional and global left ventricular function, additional end-points may be at least as important, including improvement of heart failure symptoms, exercise capacity and long-term prognosis. Di Carli et al., employing fluorine-18-fluorodeoxyglucose and positron emission tomography, demonstrated a direct relationship between the pre-operative extent of viable tissue and the post-operative improvement in exercise capacity. Moreover, retrospective analyses of patients with scintigraphically viable tissue demonstrated a low incidence of (peri-)operative events and an excellent long-term survival following surgical revascularization. In contrast, patients with viable tissue who
were treated conservatively exhibited a high cardiac event rate during the follow-up period[13]. Pooling of the data from the five prognostic studies using fluorine-18-fluorodeoxyglucose and positron emission tomography in 549 patients with chronic coronary artery disease and left ventricular dysfunction showed that hard events (cardiac death, myocardial infarction) occurred in 9% of the patients with viable myocardium who underwent revascularization and in 42% of the patients with viable myocardium who were treated medically[12]. Hence, the findings in the study by Baer et al.[13] and the results of many other reports[13–15] must lead to the conclusion that viability assessment in patients with chronic coronary artery disease and depressed left ventricular function appears useful in the prognostification and guidance of subsequent treatment of these patients. Various techniques are now available, each probing a different feature of the dysfunctional but viable myocardium. More sophisticated and accurate tools, such as dobutamine magnetic resonance imaging and dobutamine transoesophageal echocardiography, make non-invasive viability assessment feasible in nearly all patients with reduced left ventricular function and may allow even more precise identification of viable tissue. Appropriate application of these advanced imaging modalities will result in improved prognosis and better guided clinical management.

**Table 1** Different characteristics of viable tissue versus the different techniques to assess viable myocardium

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Technique</th>
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<tbody>
<tr>
<td>Myocardial glucose utilization</td>
<td>Fluorine-18-fluorodeoxyglucose</td>
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<tr>
<td>Cell membrane integrity</td>
<td>Thallium-201</td>
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<tr>
<td>Intact mitochondria</td>
<td>Technetium-99m sestamibi/tetrofosmin</td>
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<tr>
<td>Contractile reserve</td>
<td>Dobutamine-echocardiography/magnetic resonance imaging</td>
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**Figure 1** Accuracies of the different viability techniques to predict improvement of regional left ventricular function post-revascularization. FDG=fluorine-18-fluorodeoxyglucose; TI-201=thallium-201 (including rest-redistribution and reinjection imaging); MIBI=technetium-99m sestamibi; D-TTE=dobutamine stress transthoracic echocardiography; D-TEE=dobutamine stress transoesophageal echocardiography; D-MRI=dobutamine stress magnetic resonance imaging.

References


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Cell adhesion molecules, simvastatin and hormone replacement therapy, in coronary artery disease

See page 975 for the article to which this Editorial refers

The paper by Sbarouni et al. in this issue[1] deals with several very timely topics. First of all, the magnitude of lipid lowering obtained by hormone replacement therapy is less than with established simvastatin therapy, but hormone replacement therapy is also associated with significant lowering of total cholesterol as well as LDL-cholesterol. Secondly, hormone replacement therapy is associated with a decrease in lipoprotein(a), an effect which in the clinic might imply a reduction in atherogenesis and an improvement in spontaneous thrombosis. These effects were not obtained by simvastatin. The main difference in action was, however, seen in relation to the soluble adhesion molecules ICAM-1, VCAM-1 and E-selectin, all claimed to be involved in the inflammatory response leading to increased atherogenicity. Inflammatory markers have been claimed to be associated with increased risk of severe outcome in angina pectoris, such as myocardial infarction and sudden death[2]. The study is small but meticulously conducted and the results are in accordance with other findings.

However, the study deals with surrogate end-points and it may be superfluous to remind readers that cardiological practice has repeatedly been misled by such observations. The most flagrant examples are the studies with prophylactic antiarrhythmic therapy after myocardial infarction. The HERS study (Heart Estrogen/progestin Replacement Study) also illustrates this since hormone replacement therapy in this study was not associated with improved prognosis in a mixed group of women with coronary heart disease, which was in contrast to several impressive observational studies. The study of Sbarouni et al.[1] underlines that the hormone replacement therapy issue is not yet resolved and that further experimental and clinical studies need to be done. If these findings were concurrent with clinical effects, leading to a slowing down of the atherosclerotic process and a reduction of the risk of severe manifestations of the disease, both therapeutic and preventive strategies would appear. That there is reason to believe that this might be the case is the fact that women with angina pectoris have better prognosis than men, even if adjustments are made for age and concomitant diseases[3].

The female hormones may be positive modulating factors and reduce the effect of situations eliciting an acute event. The right patient population and treatment has yet to be identified. It may be pertinent to stress that hormone replacement therapy given with the purpose of improving prognosis in women with coronary heart disease is quite complicated, since the other hormonal aspects need to be taken into account, i.e. the risk for endometrial and breast cancer as well as venous thrombosis. These considerations must also be taken into account when cost-effectiveness of such treatment is discussed. Also, in a priority setting other measures for preventing a negative outcome of the disease are much more evidence-based and cost effective. From a clinical point of view, this study however, confirms the recommendations that women already on hormone