EDITORIAL

Left ventricular remodelling after myocardial infarction: importance of residual myocardial viability and ischaemia

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Development of left ventricular remodelling after acute myocardial infarction is a complex process influenced by many factors, some of which are yet to be elucidated

During the past two decades, it has become increasingly well acknowledged that a large, transmural acute myocardial infarction (AMI) may result in complex alterations in the architecture and function of the left ventricle (LV), involving both the infarcted and non-infarcted zone. These alterations, usually referred to as "LV remodelling", can profoundly affect the patient's prognosis.

From the clinical viewpoint LV remodelling is a dynamic process, starting in the acute phase with infarct expansion—that is, rearrangement of wall structure—leading to myocardial thinning and lengthening, and progressing to LV dilatation and hypertrophy.[1] The remodelling process has regional and global effects on wall thickness and chamber size, as well as on shape and function.[2] Patients who develop LV dilatation following AMI have significantly reduced survival. In fact, LV volume is the single most important predictor of survival in patients with coronary heart disease.[3] Furthermore, Gaudron and colleagues demonstrated that LV dilatation following AMI precedes deterioration of exercise performance and plays an active role in the development of chronic heart failure.[4] They also showed that predictors of progressive LV dilatation and chronic LV dysfunction include ventriculographic LV size, LV ejection fraction at day 4 after AMI, infarct location (especially anterior), stroke index on day 4 after AMI , and TIMI grade for the infarct related artery (IRA). The relative contribution of these factors is unknown, but the patency of the IRA assumes particular importance because it is a risk factor that is amenable to intervention.

CLINICAL IMPORTANCE OF SUSTAINED PATENCY

Early evidence of the clinical importance of sustained patency of the IRA comes from studies of spontaneous reperfusion conducted before thrombolytic treatment became widely established. Jeremy and colleagues found that in patients assessed 30 days after AMI, LV dilatation occurred uniformly in patients with persistent occluded IRAs but only rarely in patients with patent IRAs.[5] It is now widely acknowledged that early reperfusion treatment improves survival by limiting infarct size, and thus preserving LV function. However, several studies have shown that the improvement in survival of patients with sustained IRA patency is greater than expected on the basis of improved global LV function alone.[6] It has been proposed that, in addition to time dependent myocardial salvage, beneficial effects of reperfusion therapy include attenuation of LV remodelling and promotion of electrical stability that reflect time independent effects of an open IRA.[7] In short, full patency of the IRA is crucial for reducing both infarct expansion in the early phase of infarction and LV enlargement later on.[8]

There is also increasing evidence to support the use of late reperfusion therapy—that is, after the six hour time window, and thus beyond the time frame for myocardial salvage. Furthermore, studies looking at residual stenosis or reocclusion after reperfusion therapy support the efforts to establish full patency of the IRA and to maintain patency in the long term. A subset analysis of the APRICOT trial (which evaluated the efficacy of antithrombotics in preventing reocclusion) demonstrated the deleterious effect of reocclusion without reinfarction, in terms of increased LV dilatation, combined with a lack of improvement in both global and regional LV function.[8] Apparently, an open IRA may provide a scaffold for the necrotic myocardium that maintains structural integrity; this limits distensibility of the infarct zone and, therefore, the extent of dyskinesis, obviating LV dilatation.[9] Finally, late reperfusion may help to preserve a small rim or even islands of viable epicardium that may be sufficient to attenuate infarct expansion.[10] In fact, the degree of transmurality is pivotal in this respect and appears to be an important predictor of infarct expansion.

LV WALL THICKENING AT REST

At rest, most of LV wall thickening reflects thickening of the inner layer of the myocardium, while the middle and outer layers contribute only moderately and minimally, respectively. Thus, necrosis predominantly affecting the inner layer may lead to significantly diminished wall thickening at rest. Although the middle and outer layers thicken little at rest, they thicken more with catecholamine stimulation and thus contribute more

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Abbreviations: AMI, acute myocardial infarction; APRICOT, anti-thrombotics in the prevention of reocclusion in coronary thrombolysis; IRA, infarct related artery; LV, left ventricle; TIMI, thrombolysis in myocardial infarction

to overall wall thickening during dobutamine stimulation.[11]

The presence of dobutamine responsive wall thickening may therefore indicate the presence of viable myocardium in the middle and outer layers of the LV wall. It is conceivable that viable myocardium at this particular level of the LV wall may eventually attenuate LV remodelling. This hypothesis was tested by several investigators[12–14]; they unanimously demonstrated, using low dose dobutamine echocardiography, that the absence of residual infarct zone viability in patients with first AMI was indeed an independent predictor of LV remodelling, despite a patent IRA and absence of residual stenosis.[12] Furthermore, they also demonstrated that infarct size, as assessed by the wall motion score index during low dose dobutamine echocardiography, was significantly related to subsequent LV remodelling in contrast to the wall motion score index at rest. This finding is not surprising as wall motion abnormalities at rest may be caused by myocardial necrosis and/or stunning. In the latter case there may be contractile reserve which can be demonstrated by dobutamine.

Thus, the extent of wall motion abnormalities during low dose dobutamine represents the extent of myocardial necrosis (true infarct size) better than the wall motion abnormalities at rest. In fact, the wall motion score index at rest was similar in the group with and without subsequent LV remodelling.[13 14] Nijland and colleagues[14] also demonstrated that the number of pathological Q waves on the ECG was another independent predictor of LV dilatation, although Q waves are neither sensitive nor specific for infarct transmurality.

In this issue of *Heart*, Coletta and colleagues demonstrate once again that contractile reserve within the infarct zone obviates LV remodelling[15]; in contrast, an ischaemic response at high dose dobutamine—that is, deterioration of the wall motion score of ≥ 2 grades either in or outside the infarct zone—was strongly related to subsequent LV remodelling. Apparently, myocardial necrosis is not a prerequisite for remodelling and can be initiated by regional myocardial dysfunction (hibernation) on the basis of severe coronary stenosis. Indeed, multistage dobutamine stress echocardiography has been shown to be safe and very reliable in detecting residual stenosis of the IRA and multivessel coronary artery disease during the first week after AMI.[16]

SUMMARY

Development of LV remodelling after AMI is a complex process influenced by many factors, some of which are yet to be elucidated. Multistage dobutamine stress echocardiography can be performed at the bedside and early after onset of AMI. This enables the clinician to identify the patient prone to subsequent LV remodelling, and thus to refine risk stratification in seemingly uncomplicated AMI at low cost—a necessity in this cost conscious era.

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