The achievement of adequate and prompt myocardial reperfusion in acute myocardial infarction (AMI) is the most important determinant of recovery of ventricular function at follow-up. This explains the great attention given to the so-called no-reflow phenomenon, which is associated with extensive myocardial damage and a high prevalence of future cardiac events after AMI. The no-reflow phenomenon has been clinically demonstrated first by the thrombolysis in myocardial infarction (TIMI) trial and subsequently studied by other invasive imaging methods such as intra-coronary myocardial contrast echocardiography, intra-coronary Doppler ultrasound, TIMI frame count, and myocardial blush grade. Recently, non-invasive techniques as intravenous myocardial contrast echocardiography and trans-thoracic coronary Doppler ultrasound have been introduced to detect and monitor dynamic changes of reperfusion over time. Other non-imaging methods are based on ST segment resolution at serial ECG monitoring and enzymatic washout curve.

The paper by Yawakura et al., published in this issue of the European Heart Journal, replicates previous experience using intra-coronary Doppler ultrasound to demonstrate that resting transthoracic coronary Doppler ultrasound may disclose a typical pattern of no-reflow, which is characterised by low peak systolic flow velocity, high diastolic peak flow velocity and short deceleration time of the diastolic flow velocity curve in the left anterior descending (LAD) coronary artery. In the authors' hands, deceleration time was superior to TIMI frame count, ST resolution, and creatinine kinase MB (CK-MB) washout in detecting the no-reflow phenomenon. The authors elected as the gold-standard for the assessment of no-reflow intra-coronary MCE with sonicated ioxaglate, an interesting technique introduced by Ito et al., back in 1992.

Besides being acknowledged for introducing MCE for the study of myocardial viability, which is probably the best clinical application of the technique, the Authors have the merit of promoting the use of transthoracic coronary Doppler ultrasound in AMI, an important although still underused clinical tool to non-invasively detect reopening of the coronary artery after AMI and to monitor coronary flow over time. However, data shown in this paper raises some clinical and technical questions, particularly regarding the value and the appropriate use of the employed techniques.

Is the gold standard in a bubble?

MCE is often taken tout court as the gold-standard for effective reperfusion. MCE was performed in this study by intra-coronary injection of a sonicated radiopaque compound (ioxaglate) at the time of angioplasty. There are several potential limitations to this approach that should be recognised: (1) myocardial reflow is a complex and dynamic phenomenon characterised by cyclic variations in perfusion, which may occur within the first days of AMI (intermittent reperfusion), therefore an early and single "snapshot" view by MCE may not represent the whole story of myocardial reflow. (2) Sonicated ioxaglate is hypertonic and may temporarily alter coronary microcirculation, and the bubbles are unstable and have a non-standardized concentration. Many of these bubbles are
actually larger than 20 lm and may temporarily stick in the pre-capillary bed, eventually producing a false image of "patchy" perfusion, difficult to distinguish from true reflow. (3) The reflected ultrasound energy at the air–fluid interface of the bubbles varies with the sixth power of the radius, therefore, if the bubble diameter is not well standardised, the response to the agent could be quite unpredictable.

Peak flow velocity

Based on previous experiences with intra-coronary Doppler ultrasound, the authors propose that high peak diastolic velocity is a marker of no-reflow. However, resting flow velocity is altered by drugs, such as nitrates, dilating the epicardial vessel or by localised spasm and residual stenosis, and cannot tell much more than TIMI flow grade about coronary flow. The best way to obtain a numerical value of microcirculation viability after full re-opening of the culprit artery is to measure coronary flow reserve with adenosine, which is a potent microvascular dilator having little or no effect on the diameter of the epicardial vessel. With this method, Lepper et al., found that a coronary flow reserve >1.6 detects patients with good recovery of left ventricular function after AMI.

The slope

The authors quote that a rapid deceleration time is associated with no-reflow. Unfortunately the figures shown in this paper, as well as in others with intra-coronary Doppler ultrasound, depict an unusual coronary flow pattern with a very steep early diastolic deceleration slope. There are several reasons why this unusual slope is not convincing: (1) In physics, a rapid deceleration time reflects a better patency profile of a hydraulic system, rather than increased resistance, which is clinically confirmed by Doppler-ultrasound tracings in mitral stenosis and aortic regurgitation. (2) In routine clinical practice and experimental animals, even in cases of severe microvascular damage, coronary flow velocity is characterised by a slowly decrescendo diastolic flow, with a prolonged deceleration time. This pattern reflects high microvascular resistances at rest, which are controlled by local metabolic autoregulation, At stress, coronary resistances markedly decrease, and accordingly the slope increases. In fact, in patients with normal coronary arteries, the slope increases with the administration of coronary microvasculature vasodilators, reflecting a reduction in peripheral resistances. In patients with significant coronary artery disease (i.e., with a proximal fixed resistance), the hyperemic slope inversely correlates with the severity of the stenosis, that is, the higher the stenosis (higher resistance) the lower the slope at hyperemia. (3) If a steep slope in early diastole is determined by microvascular obstruction, it is not clear why in mid and late diastole the curve recovers the normal pattern of slowly decrescendo flow. (4) There is no logical explanation why the altered slope is lost at follow-up, even in patients with persistent severe microvascular damage and depressed left ventricular function. (5) It seems that there is no continuous spectrum for the altered deceleration time, which appears to be an all-or-none phenomenon, an unusual finding in biology. (6) Surprisingly, inferior infarction does not produce an altered slope. (7) Steep deceleration slopes can be found as an artefact even in patients without myocardial infarction (Fig. 1), which suggests that it might be the result of a wall motion artefact and may be eventually exacerbated by ventricular dyssynchrony in the setting of anterior AMI. Therefore a word of caution should be given before considering the resting Doppler ultrasound slope as a reliable marker of adequate reperfusion. In fact, in this study, resting coronary Doppler ultrasound parameters correlated well with MCE, but only weakly with recovery of left ventricular function at follow-up (r=0.48), which is however the clinical proof of myocardial viability.
Which role for systole?

This paper has the merit to reset the predictive value of systolic flow reversal as a sign of no-reflow. In fact, systolic flow reversal was found in only 18% of patients with no-reflow and in 3% of those with reflow. As for deceleration time, a good explanation for the pathophysiology of systolic flow reversal is lacking, and we are again facing another possible Doppler artefact (Fig. 1). Coronary flow is inverted in systole only in the perforating branches where blood is squeezed backwards by myocardial contraction. There is no reason why coronary flow should be inverted in the epicardial artery, if not sampling very close to the origin of a perforator, particularly during AMI, when the backwards force of myocardial contraction is lost or severely depressed because of myocardial necrosis and stunning. Moreover, red blood cells move in the epicardial coronary artery according to a forward pressure gradient throughout the cardiac cycle, and it is hard to accept that systolic pressure in the distal coronary bed overcomes systolic pressure in the aorta at any time. The authors also found that patients with no-reflow had a lower systolic peak velocity compared to those with reflow, but as for diastolic flow parameters, systolic peak velocity did not predict recovery of function at follow-up either, confirming that resting Doppler parameters are not suitable for the assessment of no-reflow.

Conclusions

Transventricular coronary Doppler ultrasound is a readily available and fascinating technique at our fingertips for the non-invasive study of coronary pathophysiology in a number of clinical settings. Care should be taken however to recognize tricks of resting flow patterns; in this way we shall avoid sliding on a too slippery slope.

References