Plaque instability leading to coronary thrombosis is the underlying pathophysiology for an acute coronary syndrome (ACS). Although a superficial erosion of the luminal surface may trigger thrombosis, in most cases the rupture of a fibrous cap into a lipid core is the initial event [1]. The mechanisms leading to plaque rupture have been studied extensively. Autopsy studies have shown that plaques with disruption have much larger lipid cores and less fibrous tissue than plaques with an intact surface [2]. Cap inflammation [3] and the increased expression of matrix metalloproteinases [4] are also important determinants of vulnerable lesions.

Plaque rupture may either heal without any symptoms or lead to mural thrombosis with subsequent healing, again with no associated symptoms. Nearly 20 years ago, Davies et al. found evidence of plaque disruption on autopsy in approximately 10% of patients who died from non-cardiac causes and who had had no cardiac symptoms before the fatal event [5]. Similarly, studies using coronary angioscopy have shown that mural thrombosis - a marker of plaque instability - may persist for weeks or months after an ACS [6, 7] and may even be observed in patients with stable coronary artery disease [8, 9]. Autopsy studies have also suggested that subclinical rupture with thrombus formation may play a role in rapid plaque progression [10]. Thus, although plaque instability is the underlying mechanism for an ACS, it may also be clinically silent (non-culprit plaque rupture) (figure 1).

Multiple coronary instability has been described recently in the setting of an ACS. Goldstein et al. showed that multiple complex coronary plaques may coexist in patients with acute myocardial infarction; they found, using angiography, a single complex (culprit) plaque in 60% of patients and multiple complex plaques in 40% of patients [11]. Studies using more sophisticated techniques for the detection of plaque rupture have provided consistent results. Rioufol et al. performed three-vessel intravascular ultrasound (IVUS) in 24 patients within 30 days of an ACS; non-culprit plaque rupture was observed in 79% of cases [12].

While the superiority of IVUS for the diagnosis of plaque rupture is recognized unanimously, coronary angiography remains the technique used in the context of an ACS in most centres. In a study by Gilard et al., published in this issue of Archives of Cardiovascular Diseases [13] the authors have analysed the value of coronary angiography in the detection of non-culprit plaque rupture, with IVUS as the gold standard. Among 105 IVUS-detected plaque ruptures, 49 were detected using angiography. The sensitivity and specificity of angiography for the detection of plaque rupture were 40% and 97%, respectively, and the positive and negative predictive values were 96% and 61%, respectively. The authors analysed the factors that predict detection of a plaque rupture by angiography. Proximal location was associated with excellent angiographic performance (80% of plaque ruptures detected). Not surprisingly, a wide cavity area was also associated with better detection. Interestingly, the longitudinal rupture pattern was a strong predictive factor: angiography was of excellent value in the case of counterflow cap orientation, but was of limited value in the case of flow-wise cap orientation. Coronary angiography thus appears to be an interesting technique with an excellent specificity for the detection of non-culprit plaque rupture, and the authors should be complimented for a well performed study.

One further challenge is to determine whether the detection of plaque ruptures at non-culprit sites could have clinical consequences. In the study by Goldstein et al., the presence of multiple complex plaques was associated with
an increased incidence of recurrent ACS during the first year after myocardial infarction (19.0% vs 2.6%) [11]. Angiographic detection of non-culprit plaque ruptures can therefore be used as a prognostic indicator. However, the exact mechanism by which ‘silent’ plaque disruption is associated with an adverse prognosis still needs to be clarified, and this would certainly help in designing preventive therapeutic strategies. Detection of a rupture at a non-culprit site could indicate a plaque that is at high risk of thrombotic complication; in such a case, a site-specific endovascular approach could be effective. On the other hand, one could argue that the detection of non-culprit plaque rupture(s) is merely an indicator of more extensive coronary artery disease, with multiple ‘vulnerable’ sites that have not been identified by angiography or IVUS; in this case, an aggressive medical approach attempting to stabilize the entire coronary tree would appear reasonable.

References