Editorial

Who wants his plaque sealed?

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There are some lessons to be learned from 25 years of coronary interventional cardiology. One of the most fundamental and important lessons learnt has been the need for an extensive understanding and knowledge of a specific disease process prior to the successful design of a targeted interventional treatment. The rapid development of sophisticated imaging equipment in interventional cardiology has resulted in a much better outcome for patients undergoing percutaneous interventions. The improved understanding of the pathology and pathophysiology of atherosclerosis and restenosis has resulted in the development of effective treatment strategies, e.g. GP IIb/IIIa antagonists, ADP inhibitors and coated stents. These continuing developments significantly raise the standard and safety of interventional cardiology.

The concept of plaque sealing is an example of an approach to treat coronary artery disease, which lacks this fundamental understanding of pathology and pathophysiology. Although it might be an interesting clinical hypothesis and might have the potential to fulfil the desperate wish of interventional cardiologists to stabilize the life threatening 'vulnerable' plaque the odds for success are slim. Currently, we do not have sufficient experimental or clinical information to justify such a therapeutic approach. There is only a vague knowledge about natural stabilization of vulnerable plaques. Recently, the first experimental models of spontaneous plaque rupture have been developed.\(^1^-3\) Therefore, we can expect to obtain more insight into the mechanisms of plaque rupture in the near future from better animal models.

In addition to poor experimental understanding we lack sufficient diagnostic methods to differentiate between low-grade, stable and vulnerable plaques. Thus, clinicians are currently striving for better invasive and non-invasive technologies capable of detecting subsequently which plaques will cause trouble in the future. At the moment, different imaging modalities are developed and first used in the clinical setting. Until now only electronic beam computer tomography has shown a correlation between components of plaque morphology (calcium score) and coronary events.\(^4\) The development of more sophisticated invasive and non-invasive imaging techniques, e.g. MRI,\(^5\) multislice CT,\(^6\) optical coherence tomography,\(^7\) thermography,\(^8\) will add to our knowledge of plaque morphology. In addition to these imaging techniques we will be able to use biochemical markers of plaque vulnerability, e.g. nuclear factor-κB\(^9\) or cathepsin B.\(^10\) The combination of imaging and markers may allow us to predict the fate of certain plaques and will probably be much more useful than conventional coronary angiography.

In the meantime more and more clinical data emerge revealing that plaque instability and plaque rupture are not isolated events in the arterial vasculature. A recently published IVUS study demonstrated that about 80% of patients with acute coronary syndromes possess at least one other ruptured plaque within their coronary tree.\(^11\) Another study showed a widespread activation of neutrophils across the coronary vascular bed in patients with unstable angina, regardless of the location of the culprit lesion.\(^12\) The situation is further complicated by pathological data showing that there appears to be a high number of subclinical episodes of plaque rupture with subsequent healing of the artery.\(^13\) All these observations undermine the rationale for an interventional approach and might explain the favourable
results of systemic therapies for the treatment of vulnerable plaques.

However, what we know today is that percutaneous intervention injures the artery and is a potential threat to the patient. And this seems to be the first lesson to be learned from the analysis performed by Mercado et al. published in this issue. The complication rate of percutaneous interventions seems to be independent of lesion severity and solely related to the interventional procedure. Any invasive approach for plaque stabilization must therefore be judged against the good evidence we have from pharmacological treatment strategies with statins and ACE inhibitors. The second lesson to be learned from this article is that even in recent randomised trials, using sophisticated diagnostic equipment, about 10% of patients are treated for mild (<50%) lesions. This is worrying and clearly demands better and more objective methods for the evaluation of lesion severity, e.g. pressure-wire or IVUS. As a further limitation it could well be that due to the selection of the study population this analysis is unable to provide a definite answer to the question if the concept of plaque sealing is indeed a useful one. Obviously, most of the patients with mild coronary lesions (≤50%) were treated because the investigator overestimated lesion severity. Therefore, a mild lesion was mechanically treated like a more severe lesion, which means high-pressure inflations, bigger balloons and stents. It is quite possible that plaque sealing will require a novel interventional strategy, different to that used for more severe lesions, i.e. low pressures, different balloons and stents. The third interesting issue to be mentioned is the comparable outcome after balloon angioplasty and stent-implantation of mild lesions in this study, an observation that deserves further experimental investigation. The new generation of drug eluting stents may play a potentially important role in the development of the concept of plaque sealing. Stents as a platform for local treatment of the whole artery or even the whole coronary tree might be a suitable therapeutic option in the future.

In conclusion, the concept of plaque sealing may be a sound option for a considerable clinical problem. The idea of an interventional approach to stabilize vulnerable plaques should not be buried due to an early attempt that lacks scientific justification and is based on a highly speculative concept. We have learned from recent developments in interventional cardiology that it will need more experimental data, improved diagnostic techniques and additional time to develop a definitive solution for vulnerable plaque stabilization.

References