

Looking beyond coronary artery stenoses

Dr Vincent Maher

Since the advent of coronary angiography, angioplasty and coronary artery bypass surgery, the coronary artery stenosis has gained prominence among clinical ailments. The degree of stenosis, their number, distribution and complexity has become a science, which has enthralled cardiologists and cardiac surgeons for years. Even patients have become enchanted by their stenoses as they proudly announce their quadruple bypass to lesser mortals with simple single or double bypass operations. Those who have only had a stent placed remain quiet in these circles, and anxiety prevails among patients whose stenoses have not been revascularised. It is not surprising, therefore that the degree of coronary stenosis is given so much respect, but is this justified?

Stenoses

Narrowing or stenoses in the coronary tree are detected in vivo using coronary angiography (Figure 1). The usual cause of stenoses are advanced atherosclerotic plaques. However, coronary artery spasm and mural thrombus may also account for the luminal narrowings seen on angiography. Although we use the term coronary angiography, the correct terminology should be coronary luminography, as we only see the shape of the coronary lumen. One can only surmise what the underlying vascular surface may actually look like. It is even more difficult to contemplate what lies beneath this surface. Such guesswork is akin to trying to ascertain the rock composition below ground based on the topography of the land.

Post-mortem studies have shown that the earliest features of plaque development are present from infancy. These studies have also highlighted that those with higher cholesterol levels have more rapid plaque development.

Plaque growth advances with age and it is frightening to think that the average 40-year old man has 35% of his coronary arterial surface covered by non-intrusive plaques.

Plaque rupture

In most patients with stable coronary artery disease, the stenoses seen on angiography reflect intrusive atherosclerotic plaques. In recent years our understanding of the behaviour of these plaques has grown enormously. Rather than consider plaque-induced stenoses as static, we now know that plaques and stenoses are more dynamic structures. In the early 1960s, plaque rupture was recognised in the coronary tree of individuals who had suffered from fatal myocardial infarctions. However, it was not until the early 1990s, that the association of plaque rupture and cardiac events was more generally accepted. What helped link these processes was that the pathological features of ruptured plaques as seen post mortem were evident on angiography. In the thrombolytic era, it was possible to compare angiograms pre- and post-thrombolysis which revealed silhouettes of plaque craters and torn fibrous caps dangling in the arterial lumen. Confirmation that these features represented plaque rupture arrived following the introduction of coronary angiography where the lesions could be viewed directly.

One of the most interesting observations of these angiographic studies was that the lesions responsible for cardiac events did not appear to be very tightly stenosed following thrombolysis. It was not known if this simply meant that a large portion of the ruptured plaques had embolised downstream, or that the plaque that ruptured was not tightly stenosed to begin with. Support for the latter hypothesis came from studies in patients who by

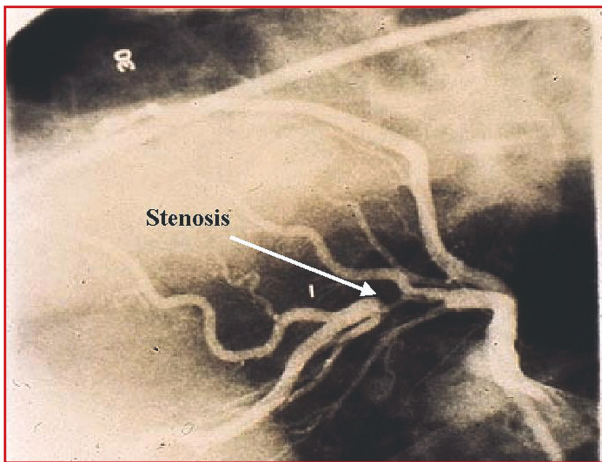


Figure 1.

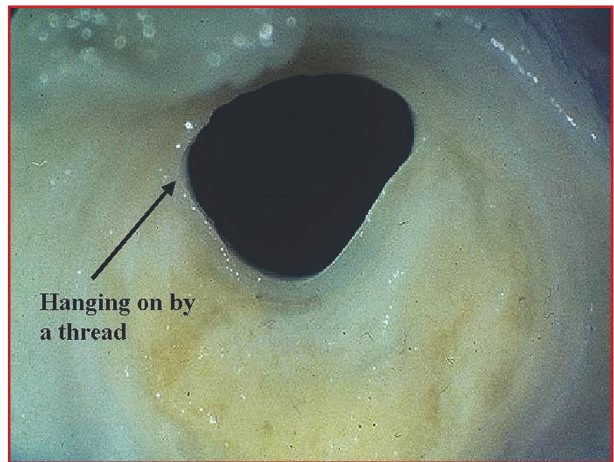


Figure 2.

chance had angiograms a short while prior to their infarctions. In this way it was possible to compare the angiograms pre- and post-infarction and determine which angiographic features could herald the occurrence of plaque rupture. To most peoples' surprise it was not the tightly stenosed lesions of greater than 70% that accounted for the majority of infarctions. In fact, 66% of all plaque ruptures occurred in lesions that were less than 50% stenosed pre-infarction. Thus it is not possible to predict the site of plaque rupture. However, the greater the number and degree of stenoses present the greater the risk of plaque rupture at some site in the coronary artery tree. Therefore, detection of stenoses, whether invasively using angiography or non-invasively through stress testing, is a useful predictor of future cardiac events.

There has also been a keen interest in the factors that trigger plaque rupture. The more frequent occurrence of heart attacks in the early morning hours and the association of some infarctions with energetic activities has generated interest in haemodynamic forces triggering plaque rupture. However, a couple of recent studies have con-

firmed that over 90% of infarctions occur in individuals who were not involved in any activity at the time.

How can we explain this phenomenon? Histological studies of coronary plaques that are prone to rupture have revealed certain common characteristics. They usually have a large lipid pool covered by a thin fibrous cap that has marked cellularity. Plaque cellularity plays an important role in weakening the fibrous cap over plaques. The main cell types in the fibrous caps are macrophages, which secrete digestive substances that erode the fibrous cap, fibroblasts, which produce collagen to re-strengthen the fibrous cap and T lymphocytes, which produce interferon that inhibits fibroblasts from repairing fibrous caps. When the balance leans towards more macrophages and T lymphocytes and less fibroblasts, there is a shift towards fibrous cap digestion. Such cellular changes may occur due to infections or inflammatory processes in plaques. This results in a weakened cap that can rupture with a minimal stress. It is therefore understandable why most cardiac events occur without any perceived trigger. When you think of plaque fibrous caps like this, you realise that our lives

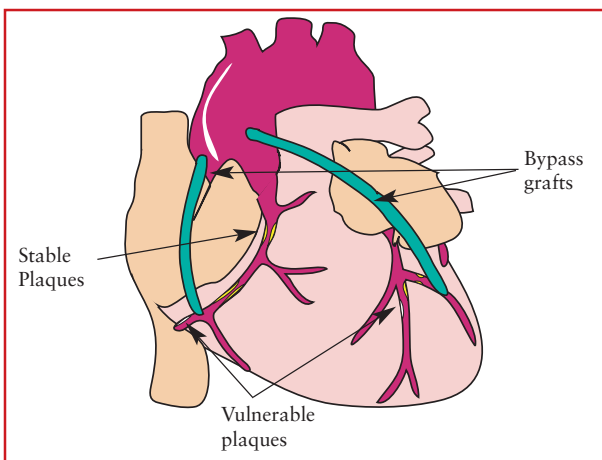


Figure 3. Difficulty in dealing with coronary plaque vulnerability

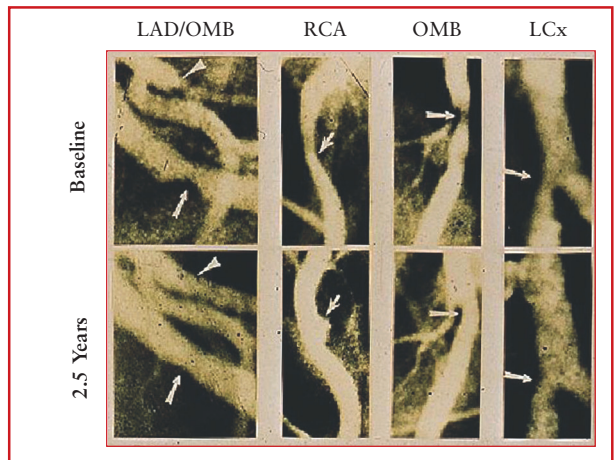


Figure 4. Regression or shrinkage of plaques after cholesterol reduction

can literally be hanging on by a thread! (Figure 2).

Based on the above-mentioned observations regarding stenoses, one can appreciate that coronary atherosclerosis is a progressive disease punctuated by unheralded episodes of plaque rupture. These events occur in plaques which have no angiographic features that broadcast their instability. With this understanding of plaque behaviour, how should we manage coronary artery disease?

Management of coronary artery disease

There are a number of approaches to deal with coronary artery stenoses. We use anti-anginal drugs to improve the balance between supply and demand around stenoses, angioplasty and stenting to remove stenoses and arterial or venous grafts to bypass these narrowings. Such approaches deal with the mechanical aspects of plaque-induced stenoses. In doing so they remove symptoms, improve wellbeing and reduce the risk of ischaemic-induced arrhythmias. However, anti-anginal drugs do not generally change the course of the atherosclerotic process. Angioplasty by its nature can only give symptomatic relief and does not prevent plaque rupture. Bypass surgery provides a safety net in case of plaque rupture and vessel occlusion proximal to the site of graft insertion. Rupture of plaques distal to the site of graft insertion are not protected (Figure 3).

When a vessel is occluded it is not uncommon for collaterals to develop from neighbouring vessels. Through these collaterals, it is possible to prevent a full-blown infarction. In a sense, bypass grafts provide such a collateral blood supply.

It is therefore not surprising that the main benefits of bypass surgery are seen when one has multi-vessel proximal disease. In such a disease state the potential of neighbouring native coronary vessels to provide collaterals is very limited. This is not the case in single vessel disease, where the other native vessels are capable of providing a potential collateral safety net. In such situations, bypass surgery has been shown to have a lower impact on mortality compared to when it is performed in the presence of severe disease.

It must be remembered that all methods that improve coronary blood flow enhance a patient's wellbeing and improve their ability to exercise. These effects will inevitably have an impact on reducing the risk of plaque rupture and will indirectly benefit the overall disease process.

Stabilising atherosclerotic plaques

Despite all the great advances in methods to mechanically deal with coronary atherosclerosis, we cannot lose sight of the fact that this condition is a progressive disease process punctuated by unheralded plaque rupture. The good news is that medical knowledge has also exploded regarding

ways by which one may alter the course of coronary atherosclerosis.

There is ample epidemiological evidence to highlight the association of cardiac risk factors with cardiac events. Numerous large-scale clinical trials where cardiac risk factors were modified using lifestyle and pharmacological interventions have resulted in significant reductions in cardiac events. Many smaller coronary angiographic studies have been performed using similar risk factor interventions. These latter studies have helped elucidate the mechanisms underlying the observed reductions in cardiac events through risk factor intervention. Interestingly, very few angiographic changes were observed in these studies, despite major cardiac event reductions. This paradox can be explained by the fact that plaque stabilisation occurs with risk factor intervention. Such plaque stabilisation is not angiographically spectacular.

These trials also demonstrated that in some instances, it is possible to induce angiographic regression of atheroma (Figure 4). By inducing regression or shrinkage of stenoses, anginal symptoms and the need for anti-anginal drugs are reduced.

This brings up the question of whether or not all patients should be given a trial of aggressive risk factor intervention before any form of revascularisation is considered.

Only carefully conducted trials will prove whether or not aggressive risk factor modification is a better long-term choice than revascularisation.

In summary, coronary stenoses are merely the topographic presentation of an underlying active disease process. The correct management of coronary artery disease should involve both optimisation of coronary blood flow and stabilisation of the atherosclerotic disease process. Both approaches are essential and interdependent. So, at the end of the day, it does not matter how much or how little revascularisation one has had done, as long as coronary blood flow is optimal and plaques are stable.

Dr Vincent Maher is a

Clarification

In our Spring issue, Dr Khan Bahadur should have been cited as first author of the article 'Transoesophageal echocardiography: why and when?'. Eireann Publications wishes to apologise for this error.