

# Coronary Collaterals: A Little Give and Take, and a Few Unanswered Questions

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The human collateral circulation was described in detail in the 1930s by Charles Hudson [1]. William Fulton's work in the 1950s and 1960s subsequently showed that the human coronary circulation in both health and in disease consists of a complex pre-existing anastomotic network rather than functional end arteries and that an occluded epicardial vessel is associated with an increase in diameter of the collaterals [2,3]. These coronary collaterals can be sufficient to preserve resting left ventricular systolic function in spite of complete coronary occlusion.

There is variability amongst individuals with respect to their ability to develop a functional collateral supply. It has been shown that if an individual is able to develop a collateral supply sufficient to prevent ST-segment elevation on balloon coronary occlusion, there is an association with improved survival [4]. This may in part be explained by protection against ischaemia in the setting of ST-segment elevation myocardial infarction [5]. Although our understanding is based upon patients with sufficient symptoms to present to us and require treatment, collateral supply appears seldom sufficient to prevent the occurrence of ischaemia with myocardial stress in the presence of an occluded artery [6,7].

The physiological significance of a coronary stenosis can be assessed at the time of coronary intervention using a specialised guidewire that incorporates a pressure sensor at the distal end. At maximal hyperaemia (using adenosine), we can derive a fractional flow reserve (FFR) by comparing the difference in pressure proximal and distal to a stenosis. There is a validated FFR cut-off whereby lesions should be considered as significant and require revascularization. For patients with multivessel disease, there is large randomized trial evidence demonstrating that FFR-guided therapy has a beneficial effect on outcome, including the 'harder' end-points of death and myocardial infarction [8]. The influence of a large collateral supply on donor vessel haemodynamics and in particular, FFR merits further investigation. Collateral supply not only influences the recipient myocardium, it also influences haemodynamics in the vessel donating collaterals. As flow is proportional to the mass of perfused myocardium, if a vessel is donating collateral blood supply to an additional myocardial territory, we would expect flow in that artery to increase. As a consequence to this, conventional theory would suggest that the addition of a collateral supply to a donor vessel will increase its resistance and reduce its FFR. Bearing in mind perfusion to a collateralised segment is seldom equal to that of an unobstructed epicardial vessel and that collateral steal is a reasonably prevalent phenomenon, particularly in the presence of a diseased donor vessel [9], we do not know how large that change in hyperaemic flow would be. In addition, small calibre collaterals might act as a stenosis in series with a donor vessel stenosis, the absence of which would actually decrease, rather than increase the donor vessel FFR [10].

Our current understanding is that collateral growth of pre-existing anastomotic arterioles, termed arteriogenesis, occurs independently of an ischaemic stimulus by means of mechanical transduction of endothelial shear stress, stimulating a cascade of growth factors and inflammatory mediators [11]. An increase in shear stress would be

expected if a pressure gradient were to develop between epicardial coronary territories due to a stenosis or occlusion. Pharmacological or mechanical stimulation of arteriogenesis is an attractive goal with the potential for real clinical utility, particularly in the setting of refractory angina unsuitable for revascularization, or even with the more modest ambition of enlarging collaterals sufficiently to facilitate a retrograde attempt at angioplasty to a chronic total coronary occlusion. Thus far, pharmacological attempts to stimulate collateral growth have met with limited success [12], and the prospect of any clinical application in the near future seems slim. Exercise has been shown to stimulate invasively measured collateral function with a 'dose-response' relationship [13], a translation into any clinical benefit is yet to be demonstrated however.

We still have much to understand about the development, haemodynamic effects and potential for manipulation of the coronary collateral circulation. Further work in this area will facilitate improved decision making and possibly even novel therapies in treating patients with coronary disease.

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