A second limitation may be that our mechanical methods (balloons with jets, leaks or even needles, coated stents, etc.) are too rough for the tiny endothelial and subendothelial tissues. Despite reports about the feasibility and safety of different local drug delivery devices \cite{4–7}, their clinical effectiveness has yet to be proved. Increased risk of arterial thrombosis after local delivery of some drugs is one major issue \cite{8}, but probably the most important limitation is the greater extent of tissue injury by local drug delivery devices. This additional injury may stimulate more neointimal hyperplasia and thus counterbalance the potential benefit of locally delivered drug.

The fight against restenosis is a 20-year vicious circle. Up to now, local intracoronary drug delivery seems not to have broken this circle. New, entirely different approaches — intrapercardial drug delivery \cite{9}, radioactive stents and intracoronary radiation therapy may help break this circle in near future.

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References


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Collateral flow and restenosis: appreciating hydraulics and outcomes of percutaneous coronary intervention

See page 1776 for the article to which this Editorial refers

Wahl et al.\cite{1} have addressed the question whether patients with restenosis after angioplasty had higher collateral flow to the recipient vessel than patients without restenosis. Two hundred patients were examined and a collateral flow index was derived during balloon occlusion using aortic, distal coronary and central venous pressures. Sixty-four patients had angiographic follow-up 2 months later and were divided into two groups; 34 patients with and 30 patients without restenosis. Patients with restenosis had a higher collateral flow index at the time of coronary angioplasty than patients without restenosis. These data suggested that patients with restenosis after angioplasty had a more extensive collateral supply beforehand and that well-developed collaterals were a risk factor for restenosis.

This paper comes from a laboratory with a superior track record in coronary physiology and an established publication history for the coronary collateral flow velocity and pressure indices derived from patients undergoing intervention. The investigators are to be complimented for delving further into the haemodynamics of coronary responses to
intervention and attempting to add hydraulics as a potential risk factor for adverse outcomes. However, it is difficult to assign the designation collateral flow index ‘risk factor’ to all patients derived from only two small groups. Nonetheless, there is much merit to the discussion and early evidence to support this research. It is also important to appreciate the rationale as to why collateral flow might influence restenosis.

The support from several early studies using coronary occlusion wedge pressure\(^{2-4}\) directs our attention to the fact that if coronary occlusion pressure is high (usually >30 mmHg), then substantial and likely functional collaterals are usually present and that such patients have higher recurrence of stenosis in this territory. In the previous study\(^5\), Seiler et al. described the determination of collateral flow index \(\geq 0.30\) to be sufficient to prevent electrocardiographic signs of ischaemia, now noteworthy in view of the restenosis potential. Competing haemodynamic forces for antegrade flow at the traumatized site may alter shear rates, platelet wash-off, accumulation of thrombus and/or platelets with release of various growth factors and stimuli to endothelial proliferation, thus favouring a restenotic milieu. Such a constellation of mechanisms appears logical. The status of artery hydraulics and haemodynamics can easily and accurately be detected with pressure sensor guidewires used during the procedure. Wahl et al.\(^{[1]}\) seem to have again proven that functional collateral coronary pressure is associated with restenosis in the absence of classic anatomical and clinical differences which would otherwise account for variation between groups.

The investigators also focus our attention on coronary flow haemodynamics in a new way. In contrast to earlier studies\(^{2-4}\), in their calculation\(^5\), the central venous pressure, used to account for back filling pressures, was estimated to 5 mmHg. Is there a role for changing central venous pressure directly in some individuals to alter the collateral flow index and determine whether or not it makes a difference in subsequent restenosis? Similarly, the presence of pre-existing channels, compared with functionally, labile and acutely recruited collateral potential, has not yet been addressed. Perhaps a more complete appreciation of the coronary flow velocity index should also be included to refine the collateral flow index–outcome relationship\(^5\).

The issue of what truly constitutes restenosis, defined solely by a dichotomous 50% diameter reduction in the lumen, may also be an issue. This diameter reduction may or may not be physiologically or clinically significant so that the relationship of collateral flow index to angiographic findings of a stenosis which may not be haemodynamically significant has an entirely different implication. The haemodynamic significance can be obtained with direct measurement or demonstration of restenosis on stress testing. An examination of restenosis by groups with demonstrable ischaemia rather than simply angiographic diameter narrowing would further complement such studies, providing the haemodynamic data to support the fact that the collateral flow index may be an even more important marker of functional than angiographic result.

The limitations of this detailed physiological study are relatively few and self-evident, principally in the small study groups. Unlike fractional flow reserve for ischaemia or restenosis\(^{16,7}\), the collateral flow index does not have such a clear point to separate expected outcomes. In patients with restenosis, it was clear that the angiographic collateral grade was higher and that the collateral flow index, on average, was also higher, but the overlap of the two groups suggests additional factors may be involved. Should not those patients with the most protective (i.e. anti-ischaemic) collaterals have the highest restenosis? This particular and provocative subgroup did not distinguish itself from the overall cohort but again the numbers are small. Finally, in keeping with the higher collateral flow index association with restenosis, it would also make sense that patients with total coronary occlusion and an extraordinarily high collateral flow index should be those with the greatest restenosis rate. The subgroup of total occlusions are presumably known to have high restenosis rates, but perhaps these are erroneously attributed to morphology and abnormal tissue substrate rather than the physiology of collateral supply.

These data facilitate our appreciation and understanding of the various coronary physiological settings during interventions and, in part, the role of hydraulics in restenosis. The current data strongly support larger investigations to finalize the contention that the coronary collateral flow index is, indeed, a risk factor for restenosis. Although most interventional cardiologists eschew or avoid the prognostic potential of coronary pressure or flow measurements, the data by Wahl et al. emphasize that an appreciation of collateral haemodynamics at the time of initial intervention may lead to better patient care by early identification of patients likely to have restenosis and thus benefit from more aggressive medical or mechanical therapies when available.

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Small vessel stenting is safe, but still waiting for a well-proven antirestenotic effect

Since the first intracoronary stent placement in patients in 1986, mainly for treating acute closure, coronary stenting indications have expanded remarkably. Coronary artery stents have been shown to reduce restenosis following coronary angioplasty as compared with balloon angioplasty alone in short coronary lesions of vessels >3 mm. Other trials generally demonstrated benefits of stenting over balloon angioplasty in various other conditions. Coronary stenting is now being used in many centres in patients with focal lesions in large vessels, in total occlusions, in long lesions, in saphenous vein grafts, in acute myocardial infarctions and in restenotic lesions[1]. These achievements were made possible thanks to new and better stent designs, improvements in stent implantation techniques and effective antiplatelet therapy with a low rate of stent thrombosis. However, the role of stents in other challenging situations, such as diffuse disease, small arteries, bifurcation lesions, and within heavy calcification, is less clear.

It is estimated that in 30–40% of all interventions the reference vessel diameter is less than 3 mm. Women, diabetics and patients with a small surface area usually have small coronary vessels. With ongoing worldwide experience it became clear that two of the most powerful predictors of restenosis are angiographic-geometric in nature: the arterial diameter and lesion length[2–3]. The likelihood of restenosis can almost be calculated from these two parameters alone.

Using models of restenosis based on late loss/acute gain ratio for small coronary vessels, stenting small vessels may offer some advantages in the immediate and late outcome. Although stenting in small coronary arteries remains an indication subject to controversy, it is currently performed in a significant number of procedures. In fact, even in strictly controlled clinical trials where only arteries of 3 mm and larger are allowed[4–5], the post procedural quantitative coronary angiography analysis has revealed that a substantial number of vessels treated are smaller than the 3 mm threshold. Yet, data from prospective randomized trials that specifically address the issue of clinical and angiographic benefit in small vessels are still lacking, although various clinical trials have been initiated and are currently underway.

The results of the study by Park et al.[6] in this issue outline important data on this frequent problem faced by interventional cardiologists every day. In this study, 120 patients with type A and B lesions in small vessels (mean reference vessel diameter of 2.52 mm) were prospectively randomized into balloon angioplasty alone or elective stenting. The procedure was successful in all patients with no stent thrombosis; however, 12/60 (20%) patients in the balloon group were stented because of suboptimal results or major dissection. During follow-up there were no differences in clinical events. Angiographic restenosis at 6 months was similar (31.9% for balloon

References