The meaning of suboptimal coronary flow reserve after coronary balloon angioplasty

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The accurate and combined assessment of anatomy and physiology has expanded our confidence in obtaining an optimal balloon angioplasty result without the perceived obligation of stenting every such treated vessel. This strategy, called by some ‘provisional stenting’, permits the enhanced and patent coronary lumen to heal with an acceptably low restenosis rate, equivalent to that of a stented artery. Multiple excellent and thoughtful studies demonstrated an effective long-term result using standard balloon catheters with adjunctive modalities of intravascular ultrasound, coronary flow or pressure measurements, although at one time attractive, this approach rapidly faded into obscurity.

The reasons for ‘obligatory’ stenting prevailing over an evidence-supported, provisional strategy arose from the rapid and highly successful evolution of the stent technique, the fact that only 50% of patients could achieve the predicted outcomes of the provisional approach, and, given equal outcomes, the immediately more satisfying and ‘physician-friendly’ procedural results providing increased operator comfort when the patient leaves the lab. Thus the most common practice for today’s stent placement is to rely on visual clues to select correct stent sizing and accept implantation results, often foregoing the well-documented benefits of adjunctive modalities.

What then is the importance of coronary flow after an intervention? The initial objective of coronary intervention is to restore normal coronary blood flow and eliminate the presumed cause of the patient’s functional impairment. Normalized coronary blood flow (and reserve) coupled to a normal coronary lumen after balloon angioplasty, and even after stenting, produces better outcomes for comparable anatomy with impaired physiology. None would question the meaning of normal coronary flow reserve in this setting. On the other hand, the greatest reservation for the use of the coronary flow reserve concept in any clinical setting is the interpretation of an abnormal coronary flow reserve. Does the reduced coronary flow reserve mean there is residual epicardial stenosis unappreciated by angiography or is this the confounding influence of an abnormal microcirculation in a patient with garden-variety coronary artery disease, or is this due to diffuse coronary artery disease? This issue continues to be unraveled by dedicated interventional cardiology researchers, examining coronary flow and pressure responses under a variety of conditions and relating these findings to clinical outcomes over several years.

In this tradition, Albertal et al., and the investigators of the DEBATE I and DEBATE II studies, examine the meaning and outcome relationships of a suboptimal coronary flow reserve after balloon angioplasty. From the initial 225 patients in the DEBATE I trial, 183 patients had complete angiographic and Doppler follow-up at 6 months, with 48% (88 patients) not achieving optimal flow reserve (coronary flow reserve > 2.5). Albertal et al. found in these patients, higher baseline flow velocities before and after balloon angioplasty. At follow-up, baseline velocities remained higher than in the optimal coronary flow reserve group. Moreover, some suboptimal coronary flow reserve patients had lower maximal hyperaemic velocities after balloon angioplasty. However the maximal absolute hyperaemia was similar to that of the optimal coronary flow reserve group at follow-up. Increasing age, female gender, increasing pre-procedural baseline average peak velocity were independent predictors of suboptimal coronary flow reserve following balloon angioplasty. Furthermore, and most noteworthy, patients with coronary flow reserve < 2.5 after balloon angioplasty had a higher target vessel revascularization rate (35 vs 22%, P = 0.036), higher recurrence of symptoms at 30 days (20 vs 12%, P = 0.018), and more positive stress test results at 30 days (19 vs 8%, P < 0.038) compared to patients with coronary flow reserve > 2.5.

These findings continue to emphasize that despite adequate or even optimal angiographic appearance, the physiological response of the epicardial vessel and the microcirculation still holds a major key to the later clinical behaviour of the patient. In practice, stenting has largely eschewed the need for adjunctive measurements (except intravascular ultrasound), but even so, and as shown in DEBATE II in patients receiving stents, those with suboptimal post stent physiology are likely to have more major adverse cardiac events than those with optimal coronary flow reserve.

Why does an impaired coronary flow reserve after angioplasty have such an impact on outcomes? In some patients, an increase in basal flow velocity after the procedure was identified as the principal
mechanism of the decreased coronary flow reserve. It could be conjectured that a higher resting myocardial metabolic demand (e.g. diabetes, hypertrophy, hypertension, or diffuse disease) was present, or that the higher basal flow after PTCA was due to slow recovery from induced ischaemia. In many studies, diabetes mellitus and diffuse coronary artery disease (i.e. long lesions) are associated with higher restenosis rates, more symptoms, and more positive stress tests, despite having a widely patent lumen at the target lesion. In addition, it is now appreciated that diffuse coronary disease impairs coronary flow reserve despite having adequate treatment lumen at the target lesion obstruction.

The fact that elderly patients and female patients had more frequent impaired coronary flow reserve should not be surprising since those patients often have diffuse disease and small vessels, two conditions which would impair coronary flow reserve in the absence of an obstructed focal stenosis. A predilection for increasing severity of occult coronary disease in patients having multiple coronary risk factors might also be reflected in the female or elderly patients, as noted in this study.

A suboptimal coronary flow reserve also identifies patients who cannot achieve a maximal hyperaemia with or without an increased basal flow. Thus, an abnormal coronary flow reserve in this subgroup implicates hyperaemic failure at a specific target lesion or abnormal microcirculatory flow and/or diffuse disease contributing to this adverse physiological marker. In this context, pressure-derived FFR is crucial to separate these entities. A normal FFR excludes persistent or new epicardial obstructions and, on continuous pressure pullback, can define the extent of diffuse coronary disease.

Should the interventionalist overcome his reticence about interpreting or using coronary physiological measurements in these settings? At the moment, provisional stenting remains an academic exercise for the practising interventionalist. However, some situations merit concern and can be easily resolved. In most cases, FFR can determine whether a focal or diffuse mechanical obstruction to flow exists. This issue is pertinent when plaque shifts, side branches become compromised, or secondary lesions take on a more concerning appearance after proximal conduit enlargement. Recall that, by design, FFR cannot address the microcirculation. Coronary flow reserve will be of importance to the understanding of the mechanisms of various pharmaco- or mechanotherapies for interventions providing continuing new knowledge. Studies, such as that of Albertal et al., expand interventional science, moving the field principally from ‘body count’ research to that of physiologically based, mechanistically oriented approaches to understand important clinical outcomes and what strategies can be used to improve patient care further.

M. J. KERN
Gerard Mudd Cardiac Catheterization Laboratory,
St. Louis University Health Sciences Center,
St. Louis, MO, U.S.A.

References