Coronary Angiography
Is it Time to Reassess?
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The introduction of selective coronary angiography by Mason Sones in 1958 stands as a milestone in clinical cardiology. The procedure continues as a cornerstone in the evaluation of the coronary arteries and is indicated not only to diagnose coronary artery disease (CAD) but also to assess its severity. These data are then integrated with other clinical information to help guide treatment decisions. Traditionally, assessment of coronary lesion severity has been accomplished by a visual estimate obtained from simple inspection of the angiogram. Although this method of assigning CAD diagnosis, and more specifically attempting to quantify its severity, has long been recognized to have important limitations, simple visual estimation remains the most commonly used form of lesion evaluation and is taken by many operators to be their reference standard.

Limitations of Coronary Angiography
Limitations of visually assessing coronary artery stenoses were realized long ago, and attempts at improving this assessment followed. Using quantitative coronary angiography (QCA) improved our ability to more accurately estimate the percent stenosis of a lesion and its length, which contribute to resistance to blood flow. Although this technique is a well-validated tool for accurately and reproducibly defining coronary lesion severity, these validations were done mostly in the cine film era using high-dose radiography and high-speed filming (60 frames per second) rates. Its use, as originally validated, remains mostly in the realm of specialized research using experimental models and in clinical trials. With the transition to so-called lossless compression digital angiography, the use of lower-dose radiography, and the lower cine capture rates (15 frames per second), the information captured has been compromised. The information available with these multiple views, clinicians defaulted to estimating the maximal percent diameter narrowing in the worst view. Additionally, considerable variability occurs in the relation between myocardial flow and percent diameter stenosis, suggesting that other factors (eg, microvascular dysfunction) also operate. Nevertheless, percent diameter stenosis is most commonly used to define the presence of obstructive CAD.

Figure 1. The relationship between percent reduction in cross-sectional area (vertical axis) and percent reduction in diameter stenosis (horizontal axis) estimates, assuming a circular and symmetrical lumen stenosis. At the point of significance suggested by the arrow, the Poiseuille formula states that the change in resistance is inversely proportional to the square of the change in diameter. Beyond this point, resistance increases on the basis of $R=8\eta L/R^4$ ($R$=resistance, $\eta$=viscosity, $L$=length). Adjunctive methods of lesion assessment and their lower thresholds for significant obstruction are shown at a hypothetical percent diameter reduction. These include fractional flow reserve (FFR), minimal luminal diameter (MLD), minimal luminal area (MLA), and coronary flow reserve (CFR).

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It is important to understand that among the many factors contributing to limit coronary blood flow (eg, diastolic pressure time, microvascular resistance), the minimal luminal cross-sectional area available for flow is critically important. At rest, blood flow remains unchanged until the cross-sectional area reduction is very severe (ie, >80% stenosis) and increases resistance (Figure 1). Maximal blood flow, however, becomes impaired when the reduction in cross-sectional area approximates 50%, and this became the definition of significant CAD. This reduction in area also operates over the length of the lesion, so lumen area reduction actually represents only 1 factor in a complex geometry within a lesion that is difficult to measure in the clinical setting. For this reason, and because experimental models centered on the idealized focal stenosis, clinicians substituted an approximation of the most severe-appearing obstruction.

However, CAD patients frequently have long or multiple stenoses in the same coronary artery. Our laboratory and others have shown that compared with a single focal stenosis, multiple consecutive stenoses and an increase in stenosis length result in a greater reduction in maximal flow. Because the area reduction over the length of the complex lesion and multiple lesions was difficult to measure precisely even with

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changes (particularly the lower film rates) markedly limits the ability to select multiple, optimally filled contrast segments in several planes as required for high-quality coronary angiography to quantitatively assess the coronary lesion (QCA). Thus, classic QCA is not used in daily clinical practice. Other methods used in an attempt to improve the estimation of lumen narrowing, such as calipers, had mixed results and thus have not achieved wide penetration into routine practice.\(^{11}\)

**Contemporary Assessment of Coronary Angiography**

It has been nearly 2 decades since the clinical assessment of CAD severity has been compared with a more quantitative approach. It is unclear whether the technological advancements and adaptation of digital imaging have affected our ability to accurately discern the degree of coronary disease by visual assessment. In this issue, Nallamothu et al\(^{13}\) compared routine clinical assessment of CAD with QCA of >200 coronary lesions from randomly selected patients before percutaneous coronary intervention. They extracted the clinical assessment of each epicardial lesion from catheterization and clinical reports. Quantitative assessments of each coronary lesion were performed from the single best view by an angiographic core laboratory. The investigators then compared the findings obtained by the 2 techniques as both continuous and categorical variables.

Overall, their QCA revealed a median percent stenosis of 80% (interquartile range, 80%–90%).\(^{13}\) The mean percent diameter stenosis assessed clinically was 8% higher than that obtained by QCA. Interestingly, there was a large difference between the 2 analysis strategies for the visually assessed severe stenoses (70%–90%). Use of QCA in this group of stenoses resulted in a severity of 50% to 70% in more than one quarter of the patients. A similar trend was noted in those patients who were clinically categorized as having 90% to <100% stenosis. There were no differences according to lesion location, angiogram quality, or whether stress testing or fractional flow reserve (FFR) was performed. When viewed from an institutional perspective, the mean difference between the 2 techniques varied by as much as 2-fold (5.6% versus 11.2%). The number of patients per site is small, however, and any inferences drawn from this part of the analysis are hypothesis-generating only.

It is important to emphasize that because all of the patients studied were undergoing percutaneous coronary intervention, the mean percent diameter stenosis was 87.9±9.9% when assessed visually and 64.6±9.2% when measured by QCA.\(^{8}\) Thus, the mean difference of 8.2% from the present study seems small in comparison, and perhaps a goal of complete concordance is not realistic. It is possible, however, that the difference between visually assessed and QCA-assessed percent diameter stenosis seen in the present study differs from that seen in an earlier era because of differences in angiographic acquisition. The use of lossy compression in the digital age may in part explain the smaller difference seen in the present study.\(^{9,10}\)

The authors should be commended for approaching this topic with such scientific rigor. Although the present work is important in providing a contemporary picture of the most commonly used method for coronary lesion assessment, it should be reassuring to note that the difference between these 2 techniques appears relatively small. It suggests that the focus from these results might best be placed on quality control, and indeed, it sets a high standard for others to achieve.

It is also an important message to send to the nonmedical community. At a time when it seems that almost daily there are accusations of medical impropriety within the cardiology community, this work sends a strong message that we as a profession are policing ourselves.\(^{15}\) If these findings can be replicated in a different cohort and one without the percutaneous coronary intervention referral bias, this work could set the stage for improvements in cardiac catheterization quality control.

Once a visual estimation of CAD severity is made, it remains for the individual operator to decide on the need for further testing before choosing a treatment strategy. Clearly, the lower the category of stenosis severity is, the greater the difference between clinical and QCA lesion assessment is (Figure 2). It is in these lesions that adjunctive diagnostic strategies are likely to play the most important role. There are other tools that, when used in conjunction with the clinical assessment of CAD, can help guide treatment decisions, especially in patients with angiographically borderline (or intermediate) stenoses (eg, 40%–70%). These include intravascular...
ultrasound, optical coherence tomography, angiography, coronary flow reserve, and FFR. The first 3 methods all improve anatomic assessment of the lesion, and the latter 2 methods provide physiological evaluation of the coronary vascular disease. They all, however, involve additional time, expense, and patient risk. It is these factors, at least in part, that have allowed the simple visual assessment of lesion severity to remain the most commonly used technique to evaluate CAD.

We are moving to an era when the additional evaluation of visually assessed disease not only has already been validated but also may at some point be mandated. We have learned the value of using FFR to assess coronary lesions from the Fractional Flow Reserve Versus Angiography in Multivessel Evaluation (FAME) studies in patients undergoing percutaneous coronary intervention. Indeed, when significant lesions as assessed by visual estimation undergo evaluation by FFR, their functional significance is often far less. When percent stenosis was visually estimated to be between 70% and 90% in FAME, 1 in 5 lesions was found not to be significant by FFR (>0.80). Even in severe disease thought to be >90% occlusive, fully 4% were found by FFR not to be hemodynamically significant.16,17 FAME-2 has extended the validation of FFR to the interventional treatment of patients with stable coronary disease.18 The goal of having complete agreement between visual and QCA estimations of CAD severity is likely not reachable, but the results of the present study suggest that the gap may not be great. With ongoing evaluation such as that provided by Nallamothu et al and the use of adjunctive strategies when appropriate, our patients will continue to receive the high-quality care that they deserve.

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References

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