Evaluation of the Culprit Plaque and the Physiological Significance of Coronary Atherosclerotic Narrowings

Morton J. Kern, MD; Bernhard Meier, MD

Clues to the identification of a plaque as dangerous (ie, vulnerable to sudden activation and/or rupture) before it becomes the culprit of a major, potentially life-threatening event currently must be gleaned from studies examining plaques after the fact.1,2 Although the risk of a given plaque causing a cardiac event, in particular a myocardial infarction, is closely related to the severity of luminal narrowing (complete occlusions excepted), it is incorrect to focus exclusively on the most conspicuous segment, that is, the angiographically significant (>70% diameter narrowing) lesions that compete with a larger number of nonsignificant (<50% diameter narrowing) and, at times, apparent lesions. Because the aggregate risk of rupture associated with many nonsignificant lesions (each with an admittedly lower individual potential) exceeds that of the fewer significant lesions, a myocardial infarction will more likely originate from a nonsignificant lesion.3

In addressing atherosclerotic plaques, coronary interventionists strive to achieve the following 2 primary therapeutic goals: (1) the elimination of angina and (2) the prevention of myocardial infarction and death. The first goal may be readily achieved with revascularization, either by percutaneous coronary interventions (PCI) or coronary bypass surgery. Methods to identify and neutralize a vulnerable plaque before it produces a coronary occlusion are new and as-yet unproven, and the therapeutic approaches in some cases are highly controversial.4

To these ends, the interventionist is handicapped when relying solely on contrast angiography to identify fine details of coronary artery disease because lumenology has an inherent inability to evaluate the vessel wall, atherosclerotic plaque dimensions, composition, distribution, and morphology. Arterial remodeling confuses the determination of the severity of segmental or diffuse coronary artery disease, because only an angiographically uninvolved lumen segment serves as a “normal” reference for comparison. To move our understanding beyond angiography, this review will discuss various current and potential anatomic and physiological techniques to identify whether a coronary plaque is truly a “culprit” lesion (Table 1).

Structure and Metabolism of the Culprit Plaque

To varying degrees, an atheromatous lesion is comprised of a lipid-rich core, a cap of fibrous tissue, vascular smooth muscle cells expressing collagen and elastin that impart tensile strength to an extracellular matrix, and inflammatory cells (such as macrophages) that produce various enzymes and procoagulant factors.5,6

The fibrous cap, which is characterized by a single endothelial cell layer, may be thinned and partially eroded by both inflammatory (T-lymphocytes) and invading smooth muscle cells. Abundant activated macrophages moving into the plaque from the vasa vasmorum produce proteolytic enzymes, such as matrix metalloproteinases, that promote collagen degradation, which leads to cap disruption and the thrombogenic surface activation associated with acute coronary syndromes.6 Other plaques (or other areas within the same plaque) have a thick fibrous cap with a predominance of quiescent smooth muscle cells securely separating the lumen from the distant lipid core. In this plaque, activated macrophages account for ∼25% of the population of inflammatory and smooth muscle cells; this often testifies to earlier plaque rupture with subsequent healing.6 Stimulation of intimal proliferation seems to be a plausible mechanism that stabilizes coronary plaque.7 Smooth muscle cells engender new fibrous proteins to strengthen the cap, regulate the synthesis of interstitial collagen, and render the plaque less prone to rupture. Typically, a plaque may simultaneously have quiescent (stable) and vulnerable (unstable) regions at any given moment (Figure 1). The vulnerability of a culprit plaque is thus determined by the critical mass of the lipid core, the thickness of the atheromatous fibrous cap, and the presence of an increased population of inflammatory cells. The ability of a plaque to limit blood flow is characterized by anatomic features (eg, lumen cross-sectional area, orifice configuration, and lesion length) impinging on and disrupting luminal blood flow.

Plaque Anatomy: Use of Intracoronary Catheter-Based Sound and Light

Catheter-based techniques transmitting ultrasound or light can uniquely visualize the atherosclerotic plaque in vivo. Intravascular ultrasound (IVUS) imaging, which is superior to angiography, provides 2D cross-sectional tomographic views and, when digitally reconstructed, can display 3D images of the artery and plaque. In addition to improved
measurements of lumen plaque and vessel area (and volume), plaque constituents such as calcification, fibrous tissue, thrombus, and plaque fractures or dissections are readily identified and, in most cases, well differentiated.8 Because of its limited resolution (>100 μm even for 40 MHz systems) and the confounding influences of surrounding tissues, IVUS is currently of little use in determining the instability of subendothelial plaque components.9 The fibrous cap thickness and protruding fractures can only be visualized with difficulty.8 In contrast, arterial calcifications, associated with stable than unstable syndromes,10 are easily observed, even with low-frequency IVUS imaging. Echocardiographically identified vulnerable plaques seem to be associated with negative remodeling after plaque rupture. Ward et al11 reviewed data indicating that true arterial vessel size by IVUS rather than plaque area has a more dynamic role in arterial lumen remodeling and subsequent plaque stability.

Newer catheter-based modalities use ultrasound radiofrequency signals to gauge the elastic properties of the atherosclerotic plaque and different histological components of the plaque.12,13 By using ultrasound radiofrequency data from arterial tissue during diastole and systole, elastograms or "strain" plaque images can be constructed; these will identify hard and soft tissue component regions. In vitro studies report differentiating lipid-rich from fibrous regions within atherosclerotic plaques.12 Similarly, IVUS radiofrequency signal analysis can differentiate an atherosclerotic lipid core from surrounding vascular tissue using 30 MHz IVUS catheter signals digitized at 500 MHz from atherosclerotic coronary artery specimens in vitro.13 IVUS elastography and radiofrequency tissue analysis provide unique characterizations of plaque without the need for additional catheters.

**Angioscopy, Optical Coherence Tomography, and Raman Spectroscopy**

Using projected light through thin, flexible glass fibers, angioscopy catheters can be inserted into a coronary artery and, after blocking blood flow, can visualize the arterial surface in color through saline irrigation. Color visualization permits separation of red and/or white thrombus from yellow lipid-rich plaques in patients with acute coronary syndromes. Because of technical limitations and lack of clinical enthusiasm, angioscopy never achieved widespread use, despite observations that angioscopic thrombosis at the culprit lesions after PCI was related to adverse clinical outcomes.14 Optical coherence tomography (OCT) uses a beam of coherent infrared laser light directed and reflected within the tissue to create a detailed tissue image with an extraordinary high resolution (2 to 30 μm). It easily differentiates lipid from water-based tissues and precisely quantifies fibrous cap thickness, despite a penetration depth of only 1 to 2 mm.15 Compared with IVUS, OCT provides more detailed information to differentiate intima, plaque, and lipid pools.16 Like angioscopy, successful clinical application must overcome the low penetration depth and the blood absorbance of signal light.

Reflected laser light from tissues can also be analyzed using spectral modeling by a spectrometer. Specific spectral characteristics, called Raman spectra, identify chemical alterations in atherosclerotic tissue.17 Raman spectra can differentiate nonatherosclerotic, noncalcified plaque from calcified plaque within coronary arteries. Like OCT, the penetration depth of Raman spectroscopy is only 1.0 to 1.5 mm, but this is sufficient to examine tissue beneath fibrous caps and within the atheromatous core. Raman spectroscopy is limited by strong image artifact from background fluorescence and the absorbance of the laser light by blood. Unlike IVUS or OCT, however, Raman spectroscopy provides no information on plaque configuration and thus would likely be coupled with IVUS, angioscopy, or OCT catheters.
Activated Plaque Physiology: Catheter-Based Thermography

The inflammation and activation of macrophages in acute ischemic syndromes promote plaque rupture, thrombosis, and vasoconstriction and are associated with increased temperature within an atheroma. Casscells et al18 showed a temperature rise of up to 2.2°C in macrophage-rich areas in freshly obtained carotid endarterectomy specimens, confirming a significant correlation between macrophage density and local temperature. In human atherosclerotic coronary arteries, a 3F thermography catheter demonstrated thermal heterogeneity with a spatial resolution of 0.5 mm in the coronary arteries of 20% of patients with stable angina, 40% of those with unstable angina, and 67% of those with acute myocardial infarction.19 No thermal heterogeneity was seen in arterial emboli, or diffuse microvascular constriction, offering clinicians a complete functional description of the results of coronary interventions23 and leading to appropriate therapy for best outcomes.

Coronary Physiology: Use of Sensor Guidewire-Based Pressure and Flow

In addition to the anatomic limitations of angiography, the lack of physiological correlations for angiographically intermediate-severe stenoses (40% to 70%) facilitated the emergence of sensor-tipped angioplasty guidewire-based coronary physiological measurements as important clinical tools.20

The principles supporting the use of pressure and flow for culprit plaque assessment arise from the rheology of epicardial blood flow. An epicardial coronary artery stenosis produces resistance to blood flow with a proportionately increasing pressure loss occurring as a quadratic function of increasing flow. Coronary flow resistance varies according to the lesion length and morphology (entrance/exit angles, length, eccentricity, and luminal topography), as well as the status of the microvasculature. In addition, because net coronary flow is the result of a complex system involving both conduit and microvascular bed resistances, attempts to establish reliable physiological correspondence from only quantitative anatomic variables (either IVUS or angiography) generally failed to predict the functional response of flow through a given stenosis accurately.

Sensor-tipped angioplasty-style guidewires delivered to regions distal to a culprit stenosis can measure post-stenotic absolute coronary vasodilatory reserve (CVR), relative CVR (rCVR), and pressure-derived fractional flow reserve (FFR; Figure 2). These measurements, now in common use for both clinical and research purposes,20,21 provide an enhanced understanding of the separate functions of the epicardial, microvascular, and collateral coronary circulation.22 For example, the impact of diffuse coronary artery disease, compared with a focal stenosis, on coronary flow can be separated using CVR and FFR. rCVR, the ratio of the target CVR to CVR in an angiographically normal reference artery, examines the status of the microvascular bed. During PCI, CVR and FFR relationships may identify coronary dissection, emboli, or diffuse microvascular constriction, offering clinicians a complete functional description of the results of coronary interventions23 and leading to appropriate therapy for best outcomes.

Absolute and Relative Coronary Flow Reserve

Absolute CVR (the ratio of hyperemic to basal flow) measures the capacity of the dual system of coronary artery and supplied vascular bed to achieve maximal oxygen supply in response to a given hyperemic stimulation and is only of value when normal. To determine whether an abnormal CVR reflects abnormal stenosis physiology, the ratio of the CVR in the target vessel to that in an angiographically normal reference vessel (rCVR) can be used. rCVR assumes that global myocardial reserve (ie, the microcirculation) is uniformly responsive and distributed, nullifying the confounding effects of hemodynamics and the microcirculation. Normal CVR in young patients using IVUS demonstrated that normal arteries have values that commonly exceed 3.0. The values for CVR associated with nonobstructed coronary arteries in patients with chest pain syndromes and transplanted hearts and in normal arteries in patients with obstructive coronary artery disease elsewhere are 2.8±0.6, 3.1±0.9, and 2.5±0.95, respectively.24 In patients with coronary artery disease, target artery CVR values associated with negative ischemic testing are generally >2.0.20 rCVR values associated with unobstructed postangioplasty and stent results are >0.80,25,26

CVR in unobstructed arteries in different patients may be highly variable due to the multiple factors that can alter either basal or hyperemic flow. To improve the assessment of CVR, Wieneke et al27 measured CVR in 141 patients in 242 unobstructed coronary arteries. On the basis of a regression model, individual CVR values obtained at different basal average peak velocities could be transformed and corrected for patient age, relating them to a mean basal average peak velocity (BAPV) of 15 cm/s and age of 55 years [CVR_corrected = 2.85 × CVR_average × 10^a, where a = (0.48 × log BAPV) + (0.0025 × age)−1.16]. The transformation by the correction formula showed that only patients with diabetes had a significant decrease in the traditional CVR and corrected CVR, whereas hypertension and current smoking had no influence on corrected CVR. Use of the corrected CVR standardizes for variations in basal
average peak velocity and patient age and may discriminate between intrinsic and extracardiac factors impairing CVR.

Pressure-Derived FFR
Reducing regional tissue perfusion below the ischemic threshold (ie, the level needed to meet myocardial oxygen demand) produces myocardial dysfunction. Myocardial perfusion is directly dependent on the coronary “driving” pressure associated with vascular resistances at the 3 major control points ($R_\text{e}$: epicardial, $R_\text{a}$: arteriolar, and $R_\text{m}$: intramyocardial capillary resistance) in the coronary circulation. The myocardial perfusion pressure (aortic pressure, left ventricular pressure, or right atrial pressure) is reduced when an epicardial stenosis produces increased resistance to flow. Resistance translates energy loss into pressure loss distal to the stenosis in proportion to the flow rate. If the more distal $R_\text{a}$ and $R_\text{m}$ myocardial bed resistances are stimulated to maximal hyperemia and remain constant, then the post-stenotic hyperemic coronary artery pressure represents the maximal achievable perfusion available in that vessel.

Using coronary pressure measured at constant and minimal myocardial resistances (ie, maximal hyperemia), Pijls et al28 derived an estimate of the percentage of normal (ie, in the theoretical absence of the stenosis) coronary blood flow expected to go through a stenotic artery and called it the FFR. The FFR, calculated as the ratio of the post-stenotic or distal coronary pressure to aorta pressure (as the pressure in an unobstructed artery, ie, the theoretical normal artery pressure) obtained at sustained minimal resistance (ie, maximal hyperemia), reflects both antegrade and collateral myocardial perfusion rather than merely trans-stenotic pressure loss (ie, a stenosis pressure gradient). Because it is calculated only at peak hyperemia, FFR is further differentiated from CVR by being largely independent of basal flow, driving pressure, heart rate, systemic blood pressure, or status of the microcirculation.29 The FFR, but not the resting pressure or hyperemic pressure gradient, is strongly related to provokable myocardial ischemia (FFR<0.75) established by rigorous comparisons to different clinical stress testing modalities in patients with stable angina.21

The major concern in interpreting absolute CVR, rCVR, or FFR is the impact of microcirculatory flow impairment. In patients with a nonuniform microcirculation, such as those with myocardial infarction, neither absolute CVR nor rCVR can identify the lesion-specific nature of flow impairment because the target vessel microcirculation is presumed to be abnormal. Likewise, in other patients, when the CVR is severely blunted (eg, in severe hypertrophy, diabetes, or hypertension), the discriminatory capacity using rCVR may not permit accurate assessment of a stenosis. In patients with 3-vessel coronary artery disease, there may be no suitable reference vessel, invalidating the use of rCVR. A lesion in these situations is best assessed by FFR. In patients with abnormal microcirculation, it can be argued that a normal FFR indicates the conduit resistance is not a major contributing factor to perfusion impairment and that focal conduit enlargement (eg, stenting) would not restore normal perfusion. Caution should be applied in extending the current physiological criteria to patients with microvascular disease, acute or remote myocardial infarction, and unstable angina. Ischemic threshold values for rCVR are under review.

Physiological Techniques Differentiating Focal From Diffuse Atherosclerosis
A diffusely diseased atherosclerotic coronary artery can be viewed as a series of branching units diverting and gradually distributing flow along the longitudinally narrowing conduit length. The perfusion pressure gradually diminishes along the artery. In this artery, CVR is also reduced but is not associated with a focal stenotic pressure loss. Thus, mechanical therapy directed at a presumed culprit plaque to reverse such abnormal physiology would be ineffective in restoring normal coronary perfusion (Figure 3).

By measuring coronary velocity and reserve, quantitative angiographic coronary dimensions, and branch lengths (to estimate regional left ventricular mass) in 59 patients, Anderson et al30 found that resting blood flow velocity varied inversely with the ratio of lumen area (A) to regional mass (M). Resting average peak velocity increased 27 ±16, 33 ±11, and 37 ±20 cm/s, respectively ($P<0.06$), in patients with minimal, mild, or moderate disease. Coronary artery disease in the left anterior descending coronary artery could be categorized as minimal, mild, or moderate based on the area/ mass ratios in these 3 groups (8.7 ±4, 8.5 ±6.2, and 5.6 ±0.03 mm$^2$/100 g, respectively; $P<0.04$), indicating that a potentially insufficient lumen dimension exists for a given perfusion field in patients with diffuse, mild, or moderate coronary atherosclerosis. Such findings would likely influence decisions toward mechanical revascularization or continued medical therapy.

The Future: Assessing the Culprit Plaque With Positrons, Magnets, and Bubbles
The obvious advantages of noninvasive means to assess the culprit plaque have expedited the dramatic growth in positron emission tomography (PET),31 MRI,32 MRI and angiography,33 and microbubble contrast echocardiographic imaging.34 PET and MRI techniques can discriminate between flow impairment due to focal, localized obstructions compared with diffuse disease. Similarly, the use of microbubble contrast echocardiography is emerging as a means to assess the microcirculatory responses to flow-limiting stenoses, collateral function, and myocardial viability. A full discussion of this field may be found elsewhere.34

PET Scanning
For lesions of intermediate severity, PET-derived CVR correlates well with intracoronary Doppler CVR.35 Abnormal PET-determined coronary reserve in angiographically normal territories seems to represent early functional abnormalities of vascular reactivity or possible diffuse atherosclerotic involvement by demonstrating a graded longitudinal perfusion deficit from base to apex during hyperemic stress.36 Coupled with quantitative coronary angiographic assessment of diffuse disease37 and confirmed by PET-derived longitudinal perfusion gradients, decisions for a vigorous antiatherosclerotic risk factor reduction program over difficult or
marginally indicated mechanical revascularization can be facilitated. 38

MRI

Current whole-body MRI at 1.5 Tesla is limited by a resolution >400 μm. A catheter-based magnet coil positioned within the target vessel can resolve atherosclerotic tissue images to 120 to 300 μm, with an 80% concordance of plaque size and intimal thickness to pathological examination. 39 The high-resolution 9T MRI (spatial resolution, ~100 μm) permits examination of serial responses of atherosclerotic pathology to pharmacological and mechanical therapies40 (Figure 4).

Phase-contrast MRI has a high correlation (r>0.89) with invasive CVR determinations. 33 In 17 patients with recurrent chest pain 3 months after successful PCI, a phase-contrast

Figure 3. FFR measurements in a patient with both focal and diffuse coronary artery disease. A, Coronary angiogram demonstrating severe (>90%) proximal left anterior descending coronary artery stenosis. FFR is determined by distal coronary pressure (PD: 34 mm Hg) divided by mean aortic pressure (Pa; 90 mm Hg) and is 0.38. B, After successful coronary stenting, CVR by Doppler velocity is only 1.5. C, FFRs after stenting immediately distal to the stent and far distally in the left anterior descending artery are 0.95 and 0.41, respectively. D, Pressure wire pullback from distal to proximal left anterior descending artery shows gradual pressure recovery associated with diffuse disease.

Figure 4. A, MRI of a plaque with an intact, thick fibrous cap (uniform dark band between the bright lumen and great plaque core). B, MRI of a plaque with intact, thin fibrous cap in which dark band adjacent to the lumen is absent. Reprinted with permission from reference 32.
MRI-CVR value $\leq 2$ had 100% sensitivity and 82% specificity for detecting luminal diameter narrowing $>70\%$, respectively. After acute myocardial infarction and reperfusion therapy directed at the microcirculation, the potential to quantify coronary flow restoration will likely have substantial therapeutic implications.

### Clinical Outcomes Related to Catheter-Based Anatomic and Physiological Data

The new modalities of OCT, Raman spectroscopy, and thermography have yet to be clinically applied. Longitudinal studies relating the IVUS characterization of a vulnerable plaque to clinical outcomes have not yet been performed. Large cross-sectional IVUS lumen areas after stenting are associated with reduced restenosis. Complete and full stent strut apposition to the vessel wall (by IVUS) is associated with reduced subacute thrombosis; however, complete stent strut apposition may not occur in 30% to 40% of angiographically-guided cases. For lesions of uncertain physiological significance, IVUS lumen cross-sectional areas $\geq 3$ to $4$ mm$^2$ are associated with abnormal CVR and FFR in most patients, supporting an objective indication for intervention ($r_{CVR}$, $0.75$).

For outcomes related to physiological measurements, threshold values ($CVR < 2.0$ and $FFR < 0.75$) associated with inducible myocardial ischemia in patients with stable angina have been reproduced by many centers with several different techniques. In support of a provisional stent strategy after balloon angioplasty alone, the coupled criteria of $CVR \geq 2.5$ and $\leq 35\%$ diameter stenosis (by quantitative coronary angiography) were associated with a 6-month major adverse cardiac event rate $<20\%$. When $FFR > 0.90$ was achieved after balloon angioplasty alone, there was $<15\%$ restenosis seen at 2 years follow-up. A $FFR > 0.94$ after Wiktor stent implantation was associated with complete stent strut apposition in $>80\%$ of IVUS-documented procedures.

For clinical decision making, several studies have demonstrated $<10\%$ lesion progression requiring intervention over 1 to 2 years of follow-up, supporting the safe deferment of intervention for intermediate lesions. Table 2 summarizes catheter-based criteria for the assessment of a culprit plaque.

### The Future: Catheter-Based Culprit Plaque Assessment and Plaque Sealing

When coronary flow or pressure measurements clearly identify a hemodynamically significant obstruction, the indication for PCI is undisputed. However, many interventionists are troubled when confronted with a modest but hemodynamically insignificant plaque. The risk of an untreated plaque causing a myocardial infarction within the next 3 years increases from $2\%$ to $15\%$ as stenosis severity increases from $\leq 50\%$ diameter narrowing to $90\%$ to $98\%$. Would such a lesion (and patient) benefit from mechanical disruption with subsequent plaque stabilization?

---

**Figure 5.** Left, Left main (LM) coronary artery narrowing (arrow) in a 44-year-old man with mild dyspnea. Top right, IVUS measurements. Mean luminal areas (MLA) are $3.9$ and $9.8$ mm$^2$, respectively. Bottom right, FFR across the lesion was 0.69. This lesion is both anatomically and physiologically significant.

**TABLE 2.** Catheter-Based Anatomic and Physiological Criteria Associated With Clinical Outcomes

<table>
<thead>
<tr>
<th>Application</th>
<th>IVUS</th>
<th>$r_{CVR}$</th>
<th>$&lt;0.75$</th>
<th>$&gt;2.0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemia detection</td>
<td>$&lt;3-4$ mm$^2$ (42, 43, 45)</td>
<td>$&lt;2.0$ (20)</td>
<td>$&lt;0.8$ (25, 26)</td>
<td>$&lt;0.75$ (20, 21, 29)</td>
</tr>
<tr>
<td>Deferred angioplasty</td>
<td>$&gt;4$ mm$^2$ (45)</td>
<td>$&gt;2.0$ (20)</td>
<td>...</td>
<td>$&gt;0.75$ (21)</td>
</tr>
<tr>
<td>End point of angioplasty</td>
<td>$&gt;2.0-2.5$ with $&lt;35%$ DS (46)</td>
<td>$&gt;2.0$ (20)</td>
<td>...</td>
<td>$&gt;0.90$ (47)</td>
</tr>
<tr>
<td>End point of stenting</td>
<td>$&gt;9$ mm$^2$; $\geq 80%$ of reference area, full apposition (43)</td>
<td>...</td>
<td>...</td>
<td>$&gt;0.94$ (48)</td>
</tr>
</tbody>
</table>

DS indicates diameter stenosis. References are shown in parentheses.
The first coronary angioplasty patient presented with atypical chest pain and a negative maximal exercise test 23 years after his initial coronary angioplasty, which was performed on September 16, 1977 in Zurich (a). The initially dilated site (old) looked pristine. There was a new, nonsignificant lesion (new). The FFR was normal across both the new and the old lesion (b and c). Toward the end of plaque sealing, a 3.5 mm balloon was inflated. The nonsignificant lesion (arrow in b) yielded between 4 and 6 bar (d). Because of the unsatisfactory results with a basically unchanged stenosis and an apparent dissection (circle in d), a 3.0 x 8 mm stent was placed (e). Panel f shows the entire vessel 23 years after balloon angioplasty (1) and immediately after plaque sealing for a new, nonsignificant lesion (2).

The concept of mechanical disruption with plaque stabilization, termed plaque sealing, has great intellectual and clinical appeal but little current data to endorse its use. For example, the risk of a significant restenosis varies from ~10% for a mild lesion to ~50% for a severe and complex lesion and might be balanced against the risk of myocardial infarction given that acute PCI infarction is only a 0.7% risk of causing an infarction during the next 7 years. Data to support such an approach will need to demonstrate that, balanced against short-term complications and restenosis, plaque sealing reduces the risk of a future infarction, reduces plaque activation in the near and hopefully distant term, and favorably influences the plaque’s natural history while incorporating PCI into the diagnostic angiography, thus reducing additional procedures, hospitalizations, and cost. Figure 6 depicts a historically relevant patient example. In the future, techniques assessing plaque vulnerability may lead to PCI to augment medical therapies for mild, non-flow-limiting lesions situated proximally in large vessels.

Conclusion

Compared with angiography, catheter-based diagnostic (light, sound, MRI, thermal, pressure, flow, etc) modalities better quantify the anatomic and physiological features of a culprit plaque, can direct appropriate mechanical or medical therapies, and potentially reduce unnecessary or ineffective attempts to restore normal coronary blood flow. However, these modalities come at a price that must be weighed against the relative benefit for improved diagnostic information. Although theoretically attractive, preemptive PCI (sealing) of significant but non-flow-limiting potential culprit plaques must await further information from both catheter-based and noninvasive methods. Assessment of the culprit plaque will help achieve the ultimate goal of improving long-term outcomes in more patients with coronary artery disease at an earlier age.

Acknowledgments

The authors thank Donna Sander for manuscript preparation, Dr Bernard de Bruyne and Dr Nico Pijls for their FFR cases, and Dr Paul Hauptman for manuscript review.

References


---

**KEY WORDS:** plaque, atherosclerosis, imaging
Evaluation of the Culprit Plaque and the Physiological Significance of Coronary Atherosclerotic Narrowings

Morton J. Kern and Bernhard Meier

*Circulation.* 2001;103:3142-3149
doi: 10.1161/01.CIR.103.25.3142
*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2001 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/103/25/3142

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Circulation* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Circulation* is online at:
http://circ.ahajournals.org//subscriptions/