Pullback Pressure Gradient: Discriminating Focal and Diffuse Coronary Artery Disease Using Coronary Physiology

Improving post-PCI clinical outcomes.

By Daniel Munhoz, MD, PhD; Jeroen Sonck, MD; and Carlos Collet, MD, PhD

Stable coronary artery disease (CAD) has been studied until now as a single disease entity. The severity of CAD is assessed by the presence and extension of ischemia.[1,2] Myocardial ischemia has been proposed as the end mechanism leading to adverse clinical events.[3] Percutaneous coronary intervention (PCI) is an effective tool to treat patients with ischemic heart disease. PCI restores epicardial conductance, improves myocardial perfusion, relieve patients from angina, and reduces myocardial infarction.[4-6]

Randomized controlled trials have established the benefit of invasive functional assessment to guide clinical decision-making about myocardial revascularization in patients with stable CAD.[7,8] Fractional flow reserve (FFR) is a vessel-level metric surrogate of myocardial ischemia.[2] Beyond determining the hemodynamic significance, coronary physiology can be used to classify CAD further into two disease phenotypes, focal and diffuse disease.

The characterization of focal or diffuse epicardial disease has been commonly done using conventional angiography. Based on coronary angiograms, different definitions have been proposed aiming at differentiating diffuse and focal CAD.[9,10] However, assessing the pattern of atherosclerosis using angiography is often equivocal and has low interobserver reproducibility.[11] Moreover, studies using intravascular ultrasound have demonstrated diffuse atherosclerosis even in normal angiographic segments.[12,13] An alternative approach to estimate the degree of diffuseness of CAD is coronary physiology using intracoronary pressure pullbacks. Pullback curves depict the distribution of epicardial resistance and expose the functional pattern of CAD. Furthermore, a pullback maneuver identifies the location of pressure step-ups in the coronary vessel as targets for PCI (Figure 1).[14]

PULLBACK PRESSURE GRADIENT INDEX

The discrepancy between anatomy and physiology for lesion significance has been widely recognized.[15,16] This includes the evaluation of the pattern of CAD as either focal or diffuse. Focal angiographic disease can exhibit a diffuse pattern of pressure losses along the coronary vessel, and conversely, patients with diffuse angiographic CAD can present with focal pressure losses (Figure 2).[14] Until now, the assessment of pressure pullback curves relied on visual assessment. The pullback pressure gradient (PPG) is a novel metric that quantifies the pattern of CAD based on FFR pullbacks. The PPG incorporates the magnitude and extension

of pressure losses, providing a continuous metric from 0 to 1; values close to 0 represent diffuse CAD, whereas values close to 1 represent focal CAD.[14]

Differentiating patients with hemodynamically significant lesions into the two disease phenotypes portends clinical and therapeutic implications. Patients with focal disease have a more severe reduction in myocardial perfusion, lower FFR, and higher transstenotic gradients.[14] These features have been associated with plaque vulnerability and a worse prognosis.[17] Conversely, patients with diffuse disease have relatively higher FFR values and lower plaque stress.[17] Furthermore, treatment options differ in their ability to reestablish epicardial conductance.[18] In focal CAD, PCI restores epicardial conductance and relieves ischemia.[19] In contrast, PCI in cases of diffuse CAD results in a minor improvement in epicardial conductance and low post-PCI FFR.[20] It can be hypothesized that patients with a high PPG (or focal CAD) benefit the most from PCI. The PPG is the first metric that enables this discrimination of CAD patterns. It provides a new opportunity to improve the management of patients with CAD considered for revascularization.

CLINICAL IMPLICATIONS

In clinical practice, after a successful angiographic PCI, one-third of patients remain with a suboptimal post-PCI FFR.[21] Low post-PCI FFR has been associated with an increased risk of adverse events and cardiac death.[8,22,23] The distribution of coronary atherosclerosis at baseline (eg, focal or diffuse) is a major determinant of the success of PCI in terms of coronary physiology. The calculation of the PPG is indicated in vessels with significant hemodynamic lesions. PPG is performed using a manual pullback for 20 to 30 seconds. We've shared details on how to perform a manual FFR pullback maneuver and calculate the PPG in the catheterization video online (link: https://youtu.be/KOqKQ4GzSis).[24] Further character-

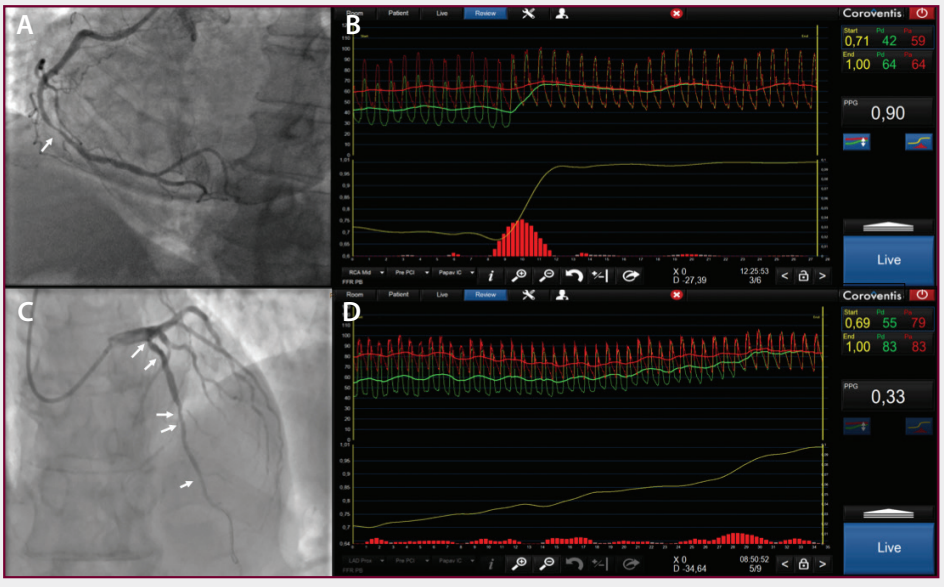

Figure 1. Morphologic and functional CAD pattern evaluation. Coronary angiography showing a right coronary artery (RCA) with angiographically focal lesion (white arrow) (A). FFR pullback of the RCA showing a focal pattern of CAD with a PPG of 0.90 (B). Coronary angiography showing a left anterior descendent artery (LAD) with diffuse lesions (white arrows) (C). FFR pullback of the LAD showing a diffuse pattern with a PPG of 0.33 (D).

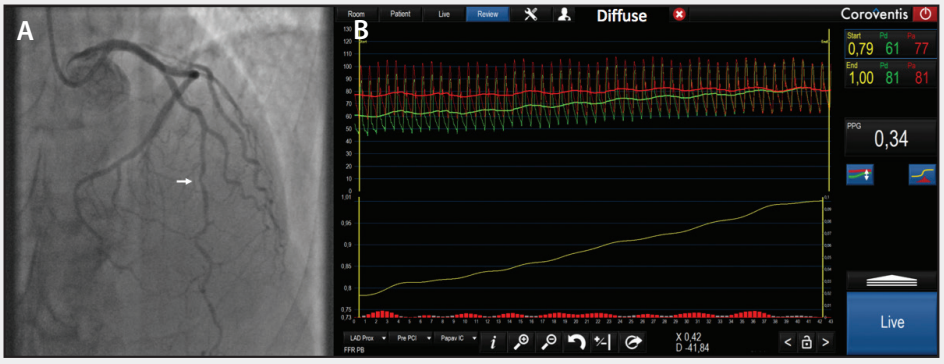

Figure 2. Morphologic and functional mismatch in the evaluation of CAD. Coronary angiography showing a LAD with a focal CAD (A). FFR pullback showing a diffuse pattern of pressure losses with a PPG of 0.34 (B).

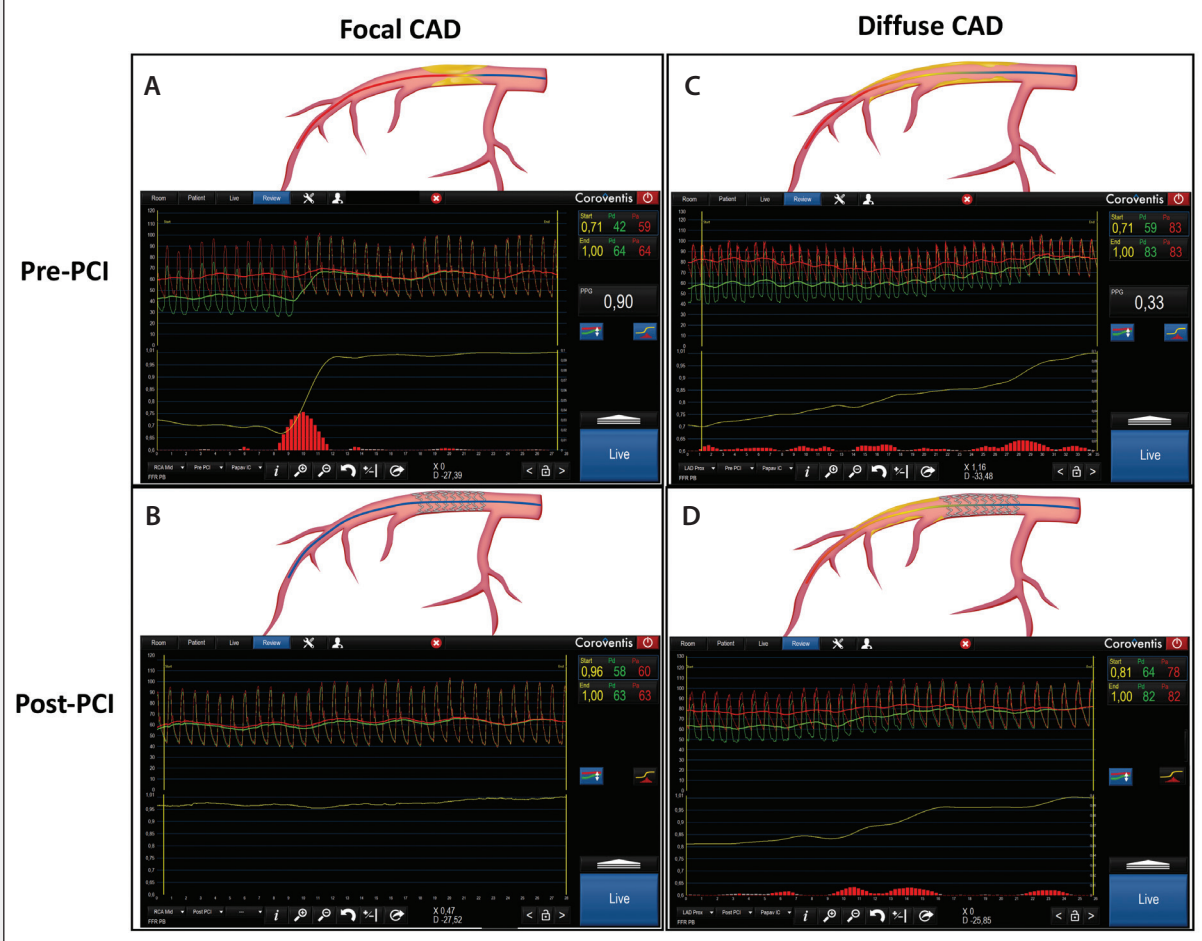

Figure 3. Interaction between the CAD pattern and PCI. FFR of 0.71 with a pre-PCI FFR pullback of focal CAD with a PPG of 0.90 (A). Post-PCI FFR pullback with distal FFR of 0.96 showing no residual disease (B). FFR of 0.71 with pre-PCI FFR pullback of diffuse CAD with schematic representation—PPG of 0.33 (C). Post-PCI FFR pullback with distal FFR of 0.81 with treated diffuse CAD showing residual diffuse disease (D).

ization of hemodynamically significant lesions into two different phenotypes aids in improved patient selection for PCI and anticipating PCI benefits. The PPG personalizes clinical decision-making and provides a prediction of post-PCI FFR before the intervention.

The adoption of coronary physiology in clinical practice continues to increase, substantiated by the evidence of clinical benefit of FFR-guided revascularization strategy.[1] The current approach that relies on detecting hemodynamic significance of epicardial lesions will be further enriched by discriminating functional CAD phenotypes and personalizing management. Coronary physiology expands from a diagnostic instrument to detect hemodynamically significant lesions to a planning tool for revascularization. PPG has been shown to predict the degree of functional revascularization, bearing the potential to enhance patient selection for PCI and improve clinical outcomes. Higher PPG at baseline results in higher post-PCI FFR. Conversely, PCI in patients with a low PPG results in lower post-PCI FFR (Figure 3).[20] Furthermore, patients with a high PPG are often free from angina after the procedure, whereas patients with

a low PPG have a higher rate of recurrent angina after PCI.[25] It can be hypothesized that patients with a high PPG have a better clinical prognosis than patients with a low PPG. This hypothesis is being tested in the ongoing prospective evaluation of the impact of the PPG index on clinical decision-making and outcomes in the PPG Global Registry (NCT04789317).

Prediction of functional revascularization represents the next frontier in interventional cardiology. The PPG adds a new dimension in the evaluation of patients considered for revascularization, enhancing clinical decision-making and tailoring the revascularization strategy. Future clinical trials will provide further insights on the value of a PPG-guided PCI strategy on clinical outcomes. ■

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