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Comprehensive Review

Coronary Physiology to Guide Percutaneous Coronary Intervention: Why, When, and How

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ABSTRACT

Over most of the history of interventional cardiology, it has been tacitly assumed that once flow-limiting coronary disease had been documented, angiography was sufficient to plan percutaneous coronary intervention (PCI) and, subsequently, to decide if an optimal procedural result had been achieved. This view has been challenged by recent studies evaluating the results of PCI with fractional flow reserve and nonhyperemic pressure ratios. Evidence has accumulated showing that suboptimal functional PCI results occur frequently despite a good angiographic result and that they are associated with worse patient outcomes. In this article, we discuss how available coronary physiology tools, either guide wire or image-based, may address this problem by facilitating better procedural planning and PCI precision and optimization.

In contemporary clinical practice, intracoronary pressure guide wires are primarily used to perform functional assessment of epicardial stenoses to determine whether revascularization is needed. In this context, it may surprise many that the first clinical use of intracoronary physiology was to assess the results of percutaneous coronary intervention (PCI), an approach first followed by Andreas Gruentzig, who used the translesional pressure gradient measured after balloon dilation to assess the functional result of the intervention.[1] With the development of thin Doppler-tipped guide wires, which provide more reliable hemodynamic measurements than over-the-wire angioplasty balloons, the focus of intracoronary physiology remained on assessing and optimizing balloon angioplasty before considering coronary stenting.[2,3] It was only after the development of the intracoronary pressure wire and the publication of the DEFER study, now more than 20 years ago, that a shift toward its current use, performing ischemia-driven revascularization, took place.[4]

However, over the last 20 years, and in parallel to pivotal studies supporting the role of physiology in clinical decision making, evidence has accumulated suggesting that not achieving a good functional PCI result is associated with worse patient outcomes.[5] Recently, the interest on using physiology to improve the outcomes of ischemia-driven PCI led to launching dedicated studies[6–10] that have clearly shown that flow-limiting coronary disease commonly remains unrecognized and untreated in PCI procedures despite an angiographic result deemed satisfactory by the operator.

In this article, we discuss the contemporary approach to guide PCI procedures using coronary physiology. This can be achieved by improved procedural planning, enhancing the precision of the intervention, and identifying and addressing the cause of suboptimal PCI results to optimize the procedure. We consider the use of physiological tools before and during PCI and also address recent studies, which to some, have raised questions about the utility of intracoronary physiology. We also outline the limitations of these studies and argue that intracoronary physiology remains critical in guiding PCI (Supplementary Appendix). In discussing the when, why, and how to perform physiological PCI guidance, we revisit not only the value of intracoronary pressure guide wires but also that of angiography-based physiology tools that derive physiological information from invasive or noninvasive coronary angiography.[11,12]

The expanding field of functional coronary assessment tools

Introduced more than 2 decades ago, fractional flow reserve (FFR) is the most widely used coronary physiology index, with demonstrated clinical value in decision making in multiple studies.[13–15] The

Abbreviations: CAD, coronary artery disease; FCA, functional coronary angiography; FFR, fractional flow reserve; iFR, instantaneous wave-free ratio; NHPR, nonhyperemic pressure ratio; PCI, percutaneous coronary intervention; PPG, pressure pullback gradient.

Keywords: coronary physiology; fractional flow reserve; instantaneous wave-free ratio and resting physiology indices; percutaneous coronary intervention optimization.

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instantaneous wave-free ratio (iFR), introduced as an adenosine-free alternative to assess functional stenosis severity, has demonstrated noninferiority with respect to FFR in decision making at 1- and 5-year follow-ups.[16,17] Several other nonhyperemic pressure ratios (NHPRs) showed a similar diagnostic yield to iFR and are now commercially available.[18] Pressure guide wire interrogation is currently recommended to assess hemodynamic relevance in intermediate-grade coronary stenosis (Class I, level of evidence A), and in patients with multivessel disease undergoing PCI (Class IIa, level of evidence B).[19] In contemporary practice, deferral of PCI is safe, once preserved epicardial vessel conductance is demonstrated with FFR or NHPR.[20] Recently, a number of trials failed to demonstrate a benefit of using FFR in scenarios like ST-elevation myocardial infarction with multivessel disease, triple vessel disease, or improving the cost efficiency of PCI.[21–23] While it is beyond the scope of this article to discuss these trials, detailed analyses of these studies are found in the Supplementary Appendix.

From a historical perspective, the arrival of the NHPR generated a renewed interest in longitudinal vessel analysis obtained over a pressure guide wire pullback. Despite having been described as early as 2001,[24] FFR pullbacks never became routinely adopted in clinical practice, largely because of the need for intravenous infusion of a hyperemic agent. This obstacle was circumvented by the arrival of the NHPR which, in addition to not requiring adenosine administration for longitudinal vessel analysis with guide wire pullbacks, was demonstrated to be effective in outlining the individual hemodynamic effect of stenoses placed in a series.[25] As discussed later in this article, this generated new opportunities for predicting the hemodynamic effect of performing PCI on a given lesion, contributing to better procedural planning. The interest in longitudinal vessel analysis with NHPR prompted the development of software solutions to provide stable pressure pullback curves, which typically show fluctuations in pressure indices caused by transient decreases in intracoronary pressure at high flow velocity locations (Venturi effect) (Figure 1). It also triggered the development of indices to quantify the degree of diffuseness of obstructive disease using FFR pullbacks, like the pressure pullback gradient (PPG)[26] and the dFFR(t)/dt[27] indices (Figure 2[28]).

A further refinement of longitudinal vessel analysis is the coregistration of the iFR pullback with angiography, which allows displaying hemodynamic information over the coronary angiogram.[29,30] By doing so, the accuracy of PCI in targeting flow-limiting coronary segments is increased, minimizing the possibility of geographic mismatch at the time of stenting.[11] The system allows prediction of final iFR results after treating specific segments in the vessel (Figure 3). Current technology allows the use of pressure guide wires as PCI workhorse wires, facilitating the performance of measurements at different stages of the intervention.

The Central Illustration summarizes the modern use of invasive physiology in 3 fundamental steps: (1) detection of ischemia-generating epicardial vessel disease, (2) revascularization strategy and PCI planning following full vessel pullback, and (3) evaluation of the physiological effects of PCI post procedure.

A shifting landscape in the use of coronary physiology to guide PCI

While evidence on the value of coronary physiology in deciding whether PCI is indicated has grown steadily over the last 2 decades, not much attention was paid to the potential benefit of using it to assess the functional result of the coronary interventions. However, hidden in trial data, there was evidence that suboptimal PCI results have an impact on patient outcomes.[5] A patient-level meta-analysis including data from 5277 patients from studies performed in the drug-eluting stent era found that postprocedural ischemic (≤0.80) FFR values occurred in 12% of patients and that, overall, there was a significant statistical relationship between post-PCI FFR values and subsequent rates of target vessel failure, target vessel myocardial infarction, and cardiac death.[31]

Of note, pivotal trials supporting the value of pressure guide wires were based on FFR measured at a single poststenotic location. We know now that longitudinal vessel analysis, obtained with a pressure guide wire pullback, provides a much richer view of the location and impact of atherosclerotic lesions on epicardial vessel conductance.[6,10,25,26,32] The relevance of this was demonstrated in the DEFINE PCI study, in which coronary vessels with a spot intracoronary measurement of iFR ≤0.89 first treated with PCI and, subsequently and once a good angiographic result had been reached, underwent physiological blinded interrogation, this time using longitudinal iFR mapping.[6] iFR pullback found that 1 in 4 patients had ischemia-generating

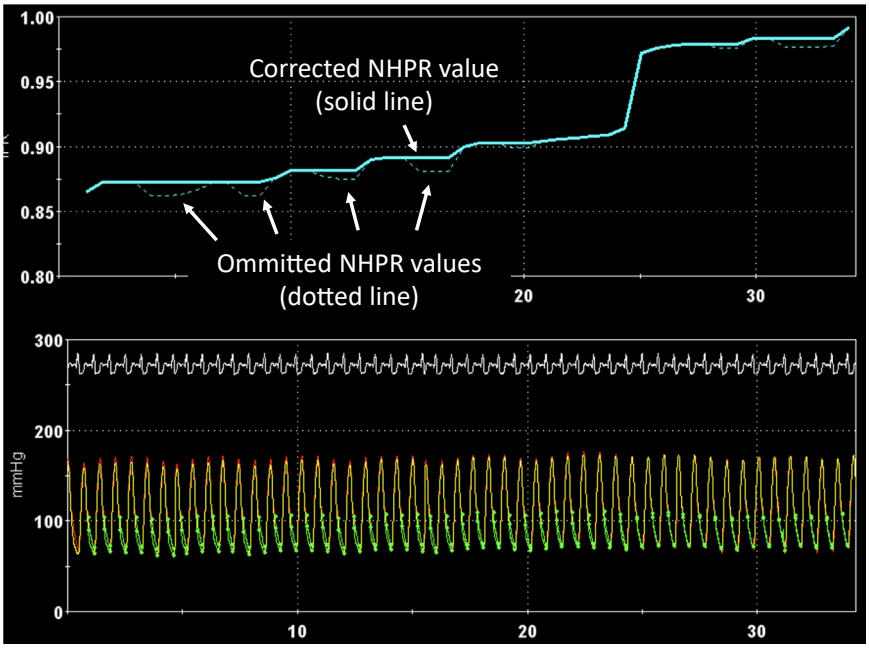


Figure 1.
Longitudinal vessel interrogation with a nonhyperemic index with dedicated analysis software. Intracoronary pressure pullback curve in diseased coronary vessels show ups and downs caused by the Venturi effect. Intraluminal pressure (Pd) decreases with higher flow velocity within coronary stenoses, causing dips of intracoronary pressure ratio values. Dedicated software for analysis of pullback curves omits such transient dips. This facilitates the interpretation of the pullback curve and the prediction of the effect of PCI on vessel hemodynamics. NHPR, nonhyperemic pressure ratio.

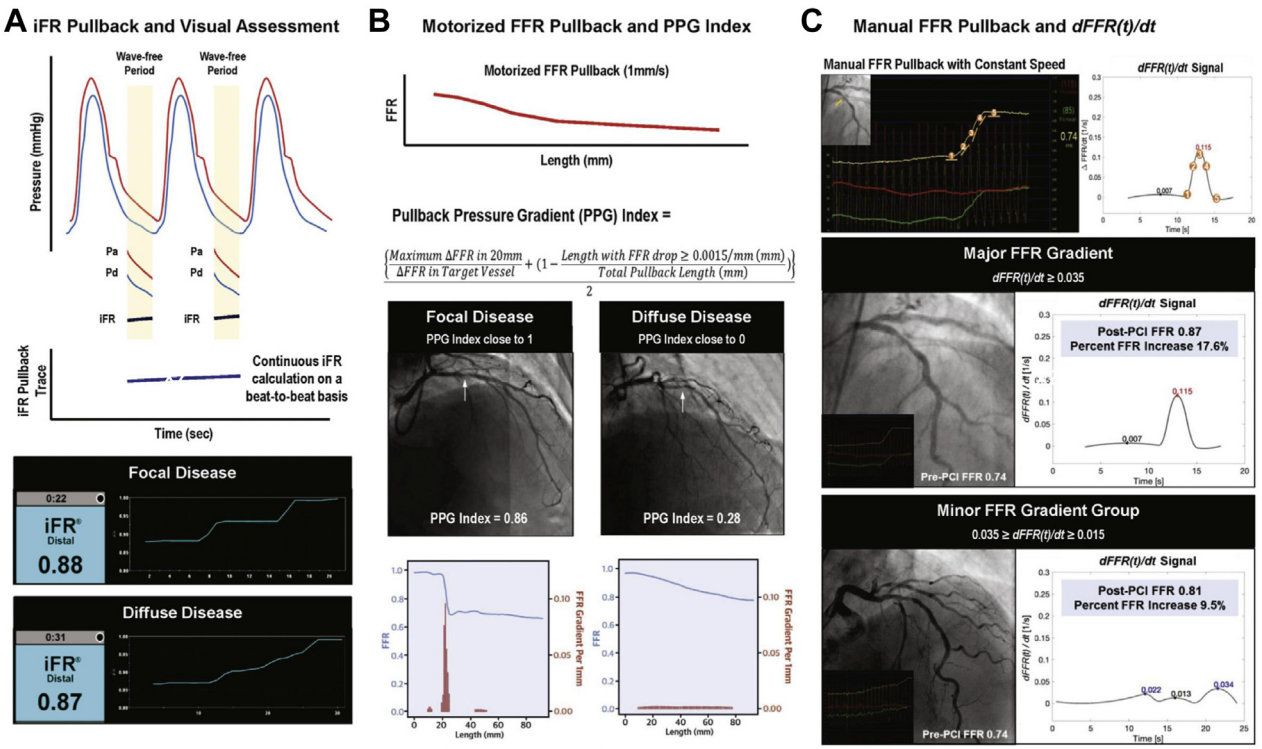


Figure 2.

Approaches to longitudinal vessel analysis with wire-based physiology tools. (**A**) iFR pullback curve displays continuous iFR values on a beat-to-beat basis along the length of vessel. By visually inspecting the step-up patterns, it is possible to discriminate focal vs diffuse disease. (**B**) Calculation of the PPG index using FFR pullback. Values of PPG index reflect focal (closer to 1) or diffuse (closer to 0) patterns of obstructive disease. (**C**) The instantaneous FFR gradient per unit time (dFFR(t)/dt) quantifies the amount of FFR changes across the target stenosis. The presence of a major FFR gradient (dFFR(t)/dt $\geq$ 0.035) predicts a good functional PCI result. Conversely, a minor FFR gradient (defined as 0.035 $\geq$ dFFR(t)/dt $\geq$ 0.015), reflecting diffuse atherosclerotic disease patterns, is associated with worse functional PCI results. FFR, fractional flow reserve; iFR, instantaneous wave-free ratio; PCI, percutaneous coronary intervention; PPG, pressure pullback gradient. Adapted with permission from Lee et al.[28]

residual disease in the treatment vessel. These findings were echoed by the TARGET FFR trial,[10] in which 29% of vessels treated with PCI had residual disease accounting for an FFR $\leq$ 0.80.

Both DEFINE PCI and TARGET FFR revealed that most cases of suboptimal post-PCI measurements are due to residual flow-limiting disease that was not tackled at the time of stenting. Although in some cases, the residual disease was not amenable to correction due to its diffusiveness, in around 25% of cases it was of a focal nature and amenable to stenting. It is easy to infer that, should the hemodynamic location of these residual flow-limiting segments be known before PCI, a different treatment strategy might be followed, either choosing longer or additional stents or, in case of diffuse flow-limiting disease not amenable to stenting, by reconsidering PCI as the adequate tool to relieve myocardial ischemia.

Under the influence of these studies, a deeper understanding has been gained of the relationship between hemodynamic coronary artery disease (CAD) phenotype and PCI effectiveness. Functional improvement associated with PCI is highest in vessels with a focal stenosis pattern on longitudinal analysis, while a diffuse physiological pattern of obstructive disease may not be successfully addressed with PCI. The

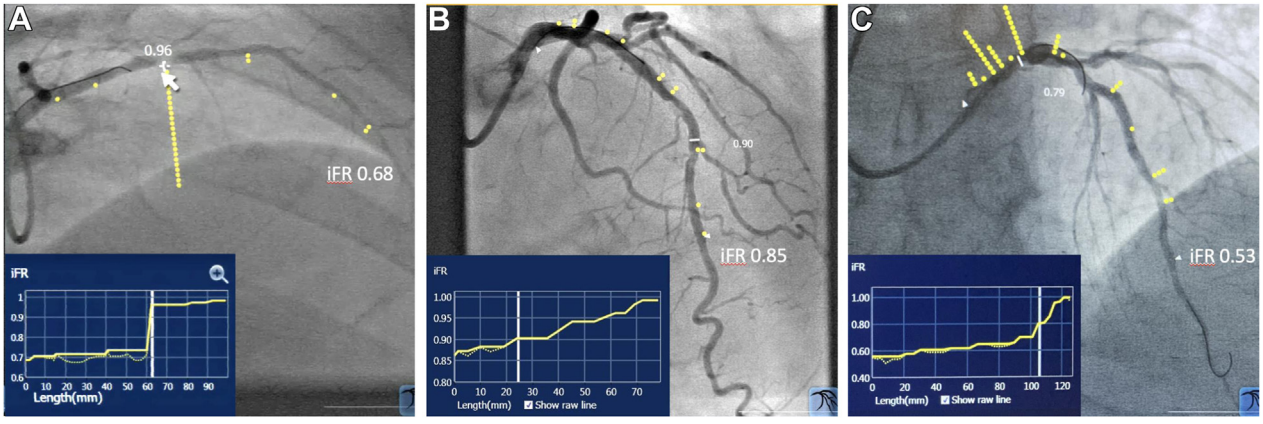
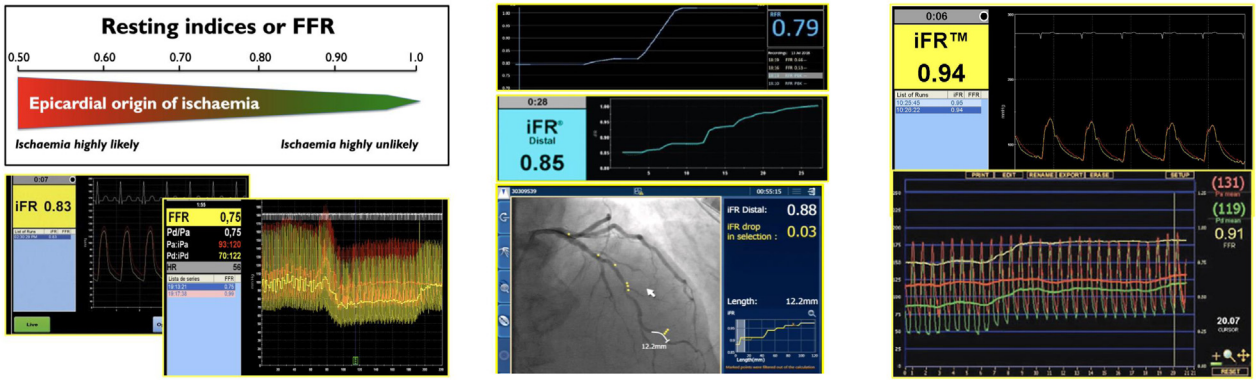


Figure 3.

Coregistration of iFR pullback with the coronary angiogram. Losses in iFR value documented over the vessel are displayed over the coronary angiogram as yellow beads, each accounting for a loss in 0.01 iFR units. Accumulation of yellow beads at a specific vessel location denotes a more focal pattern of flow-limiting disease (**A**), while a more spread out distribution of beads over the vessel is characteristic of a diffuse pattern (**B**). Frequently, a mixed pattern of focal and diffuse obstructive disease is documented (**C**). iFR, instantaneous wave-free ratio.



Central Illustration.

Stepwise approach using invasive physiological PCI guidance. Left panel: The first step of physiology-guided PCI is assessing the overall burden of ischemia caused by the vessel, and this is best achieved by placing the pressure wire as distally as safely possible within the vessel after normalization. The spot use of resting (iFR, resting full-cycle ratio, diastolic pressure ratio, diastolic hyperemia-free ratio) and/or hyperemic indices (FFR) provide a quantifiable metric that should not be interpreted strictly dichotomously, but instead seen as a probability of epicardial ischemia. Resting indices and/or FFR can be used in isolation or together in a Bayesian approach. **Middle panel:** If epicardial ischemia is unlikely following spot distal measurements (resting indices >0.95 or FFR >0.85), full vessel pullback is not needed and, following drift check, assessment can be ended. In all other cases, with borderline or more significant lesions, a full vessel pullback is essential for better understanding of when and how revascularization should be performed. Resting indices offer an advantage for pullback as they suffer less from cross-talk between lesions. At this stage, "virtual PCI" can be performed for estimation of physiological gain following stent placement. If available, physiological–anatomical coregistration further improves visual guidance (see Figure 2 for more examples). **Right panel:** Following PCI, physiological assessment should be repeated (as step 1 above) to document the results achieved by revascularization. If results are not satisfactory (vessel still shows residual flow limitation), a full vessel pullback should be repeated for a better understanding of the need for post-PCI optimization. Is the residual ischemia coming from inside the stent? Are there other flow-limiting segments? Is the potential benefit of further optimization worth the risks? Such questions can only be answered once the pattern of post-PCI physiology is clear. A final drift check confirms the post-PCI results are reliable. FFR, fractional flow reserve; iFR, instantaneous wave-free ratio; PCI, percutaneous coronary intervention.

very effect of PCI on ischemia and anginal symptoms is influenced by hemodynamic CAD phenotype. A subanalysis of the ORBITA trial demonstrated a significantly greater reduction of ischemia in noninvasive tests after PCI in patients with vessels showing an iFR-based focal CAD phenotype, compared with a diffuse phenotype.[33] A post-hoc analysis of TARGET FFR trial[34] revealed a 2-fold prevalence of post-PCI angina in patients in whom a vessel with diffuse disease CAD phenotype (defined with the FFR-based PPG index) was treated with PCI; in contrast, patients with a focal disease CAD phenotype treated with PCI had significantly higher anginal improvement and better quality of life, as judged by the Seattle Angina Questionnaire. Other studies have also reported an impact of the diffuse phenotype on patient outcomes after PCI.[32] Again, it is important to emphasize that visual inspection of the angiogram before PCI cannot establish reliably whether the dominant obstructive pattern of CAD has a diffuse or focal nature, with an overall discrepancy between visual and physiological assessment of 36%.[26]

In summary, improved pressure guide wire technology and new evidence supporting the role of physiological longitudinal vessel analysis before and after PCI have facilitated an entirely new way of addressing the key questions of when and how to perform PCI. This the following sections we shall address how this influences (1) confirming the indication and predicting the efficacy of PCI, (2) planning the best revascularization strategy from a physiological standpoint, and (3) assessing final PCI results and performing optimization of the procedure.

Confirming the indication for and predicting the efficacy of PCI

The first step of physiology-guided PCI is assessing the overall burden of ischemia caused by the vessel, and this is best achieved by, following normalization, placing the pressure wire as distal as safely possible within the vessel. The spot use of resting (iFR, resting full-cycle ratio, and others) and/or hyperemic indices (FFR) provides a quantifiable metric that should not be interpreted strictly dichotomously but instead seen as a probability of epicardial ischemia. It is possible to use resting indices and FFR in isolation or together following a hybrid approach, ie, to make decisions based on overtly normal or abnormal resting index values, and to use FFR when resting index values are near the 0.89 threshold.

It is well established that, in chronic coronary syndromes, intracoronary pressure indices are a safe gatekeeper for unneeded intervention.[20] Nonischemic FFR or NHPR values do not preclude the existence of other causes of myocardial ischemia but signify that PCI is not indicated. In cases with ischemic values, it is recommended to perform an FFR or NHPR pullback recording to allow an in-depth analysis. In addition, this will rule out the presence of pressure drift and confirm that reliable physiological measurements have been made.

If ischemic FFR or resting index values are not documented in spot distal measurements, full vessel pullback is not needed and, following drift check, assessment can be ended. In all other cases, with borderline or more significant lesions, a full vessel pullback is essential for better understanding of when and how revascularization should be performed. Resting indices offer an advantage for pullback as they suffer less from cross-talk between lesions, despite not being free from hemodynamic interaction in case of severe stenoses.[35]

The findings of longitudinal physiological analysis have been classified in a different manner. We have highlighted the 2 basic patterns indicating a focal and diffuse phenotype. However, some authors have suggested a more complex classification,[36] which includes combinations of these 2 patterns, adding as separate patterns the tandem focal lesions and a mixed pattern of focal and diffuse disease. Figure 2 provides examples of different pullback patterns with concomitant coregistration with angiography. Quantification has been also proposed using the PPG and other mathematical indices with values increasing

Table 1. Available functional coronary angiography systems.

Indices derived from invasive angiography	
QFR	• Based on good quality angiograms performed in 2 adequate angiographic projections after IC nitrate administration. • Not applicable in ostial lesions. Lack of validation in left main and major bifurcation lesions. • Allows calculation of residual QFR after removing target stenosis.
vFFR	• Overall similar characteristics as QFR.
caFFR	• Overall similar characteristics as QFR, although based on different calculation algorithms (computational fluid dynamics). • Requires sensor to acquire aortic pressure during angiography.
FFR_{angio}	• Based on 3 angiographic projections to reconstruct the whole coronary vessel.
μQFR	• May use either 1 or 2 projections. • Incorporates the effect of side branches based on Murray's law.
Indices derived from computed coronary angiography	
FFR_{CT}	• Requires external analysis (supercomputer). • Results obtained hours once the CT angiogram is available. • Includes Virtual Stenting software that simulates the effect of PCI on coronary hemodynamics.

μQFR, Murray bifurcation fractal law-based quantitative flow ratio; caFFR, coronary angiography-derived FFR; CT, computed tomography; FFR_{angio}, angiography-derived fractional flow reserve; FFR_{CT}, computed tomography derived fractional flow reserve; IC, intracoronary; QFR, quantitative flow ratio; vFFR, virtual fractional flow reserve.

from extremely diffuse to extremely focal patterns. In practice, these approaches do not modify the key goal: simulating the functional results of PCI and ensuring that a sound or acceptable physiological result can be achieved.

Different tools are available to simulate the functional result of PCI using longitudinal vessel analysis. Previous studies[25,37] have simulated the effect of PCI on a given pullback iFR curve as follows:

Predicted iFR post-PCI (iFRpred) = pre-PCI iFR (lowest value) + ∑intention to treat iFR gradient(s).

The validity of this formula has also been demonstrated for other NHPRs.[38] These mathematical approaches are facilitated when dedicated pullback analysis software correct for fluctuations in intracoronary pressure caused by the Venturi effect[30] (Figure 1). A further step in facilitating the simulation of functional PCI results is provided by iFR systems coregistering the pressure pullback with the obtained angiogram. In these cases, predicted post-iFR values are automatically delivered by scrolling over single or separate PCI target segments in a reliable way.[29,37]

Prediction of the functional results of PCI using the tools discussed earlier may help in deciding whether PCI can achieve a complete or acceptable degree of vessel revascularization. For example, in vessels with diffuse hemodynamic phenotypes, identification of those that are not amenable to PCI may lead to reconsidering percutaneous revascularization as the treatment of choice.

Planning the revascularization strategy

In parallel with testing the feasibility of obtaining a good functional result in the PCI target vessel, longitudinal physiological analysis provides valuable information for procedural planning by informing on (1) the location of lesions accounting for hemodynamic coronary impairment, and (2) whether PCI should be performed with single or multiple stents.

Even when the pressure pullback has been performed, establishing an accurate relation between the physiology curve and the angiographic location can be challenging. This is important, because geographic miss after physiological interrogation accounts for some cases of post-PCI suboptimal results. Lack of precision over stenting may leave untreated obstructive CAD. To improve this, filming the radiopaque wire tip when an abrupt change in FFR or NHPR is noted while performing the pressure pullback may help in identifying target vessel locations. Coregistration technologies, in which both physiology data (iFR) and coronary angiography images are merged and displayed together, further facilitate interpretation of physiological data and improve user interaction with physiology-guided PCI planning.[39] At this stage, "virtual PCI" can be performed for estimation of physiological gain following stent placement. Intracoronary imaging may contribute to planning of the procedure. Coregistration of intracoronary imaging with angiography may also contribute to more accurate procedures.[40,41]

Intraprocedural assessment of the physiological results of PCI

Following PCI, physiological assessment may be repeated (as step 1 above) to document the results achieved by revascularization. If results are not satisfactory (vessel still showing residual flow limitation), a full vessel pullback should be repeated for a better understanding of the need for post-PCI optimization. Is the residual ischemia coming from inside the stent? Are there other flow-limiting segments? Is the potential benefit of further optimization worth the risks? Such questions can only be answered once the pattern of post-PCI physiology is clear. A final drift check confirms the post-PCI results are reliable.[30]

The impact of procedural myocardial ischemia, embolization of plaque debris, and hemodynamic changes on physiological assessment with FFR and NHPR is not fully elucidated. From a practical perspective, postprocedural negative NHPR values may be taken as confirmative. When positive NHPR values are documented, it may be worth performing an additional FFR measurement to confirm that the NHPR is not falsely low due to increased "resting" flow from altered hemodynamics.[42]

Longitudinal vessel analysis is also recommended as the best approach to analyze final PCI results, as it helps in visualizing the distribution of intracoronary pressure loss after PCI. Suggested algorithms, such as the one used in the TARGET FFR trial,[10] proposed to limit optimization to residual focal flow-limiting segments. It must be kept in mind that, given its anatomical course when the patient is lying on the table, pressure pullbacks along the left anterior descending artery typically show a small amount of diffuse pressure loss, which is caused by hydrostatic pressure and not by obstructive disease.[43]

Role of intracoronary imaging

In performing PCI optimization, intravascular imaging is a complementary tool to physiology in optimizing PCI results, not only in providing clues as to the cause of a focal pressure loss documented at either a stented or nonstented vessel location[44] but also in deciding the best landing zones for the stent on the grounds of vessel dimensions and plaque characteristics, choosing stent diameter and length, and ensuring that proper stent apposition and expansion have been achieved. It is worth reiterating that some aspects of suboptimal stenting that can be identified with intracoronary imaging may not cause abnormal FFR or NHPR values after PCI and therefore, physiology is not a substitute to image-guided PCI.

A specific scenario for physiology-based optimization of PCI is the assessment of jailed side branches in a stented bifurcation.[45] Whenever abnormal FFR or NHPR are documented in the jailed side branch, additional maneuvers such as proximal optimization treatment or kissing balloon dilation can be performed leaving the pressure guide wire in place, so the degree of physiological optimization achieved can be gauged.[44]

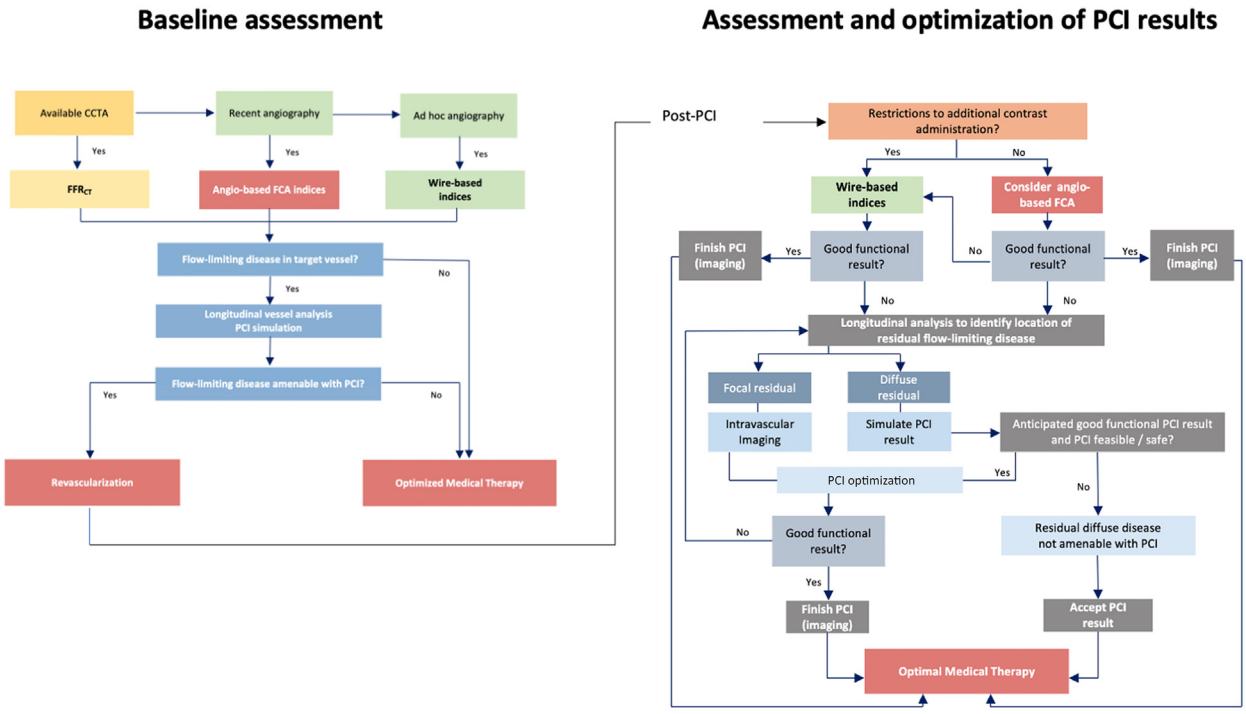


Figure 4.

Stepwise approach using invasive physiologic PCI guidance. Left panel: The first step of physiology-guided PCI is assessing the overall burden of ischemia caused by the vessel, and this is best achieved by, following normalization, placing the pressure wire as distal as safely possible within the vessel. The spot use of resting (iFR, RFR, dPR, DFR) and/or hyperemic (FFR) indices provide a quantifiable metric that should not be interpreted strictly dichotomously but, instead, seen as a probability of epicardial ischemia. Resting indices and/or FFR can be used in isolation or together in a Bayesian approach. (Middle panel) If epicardial ischemia is unlikely following spot distal measurements (resting indices > 0.95 or FFR > 0.85), full-vessel pullback is not needed, and following drift check, assessment can be ended. In all other cases, with borderline or more significant lesions, a full-vessel pullback is essential for better understanding of when and how revascularization should be performed. Resting indices offer an advantage for pullback as they experience less crosstalk between lesions. At this stage, "virtual PCI" can be performed for estimation of physiologic gain following stent placement. If available, physiologic-anatomical coregistration improves visual guidance further (see Figure 2 for more examples). **Right panel**: Following PCI, physiologic assessment should be repeated (similar to step 1) to document the results achieved by revascularization. If results are not satisfactory (vessel still showing residual flow limitation), a full-vessel pullback should be repeated for a better understanding of the need for post-PCI optimization: Is the residual ischemia coming from inside the stent? Are there other flow-limiting segments? Is the potential benefit of further optimization worth the risks? Such questions can only be answered once the pattern of post-PCI physiology is clear. A final drift check confirms that the post-PCI results are reliable. DFR, diastolic hyperemia-free ratio; DPR, diastolic pressure ratio; FFR, fractional flow reserve; iFR, instantaneous wave-free ratio; PCI, percutaneous coronary intervention; RFR, resting full-cycle ratio.

Role of functional coronary angiography

All the above discussed physiology indices rely on using intracoronary pressure wires. Over the last decade, there has been a progressive buildup of wire-free functional coronary angiography (FCA) technologies capable of identifying physiologically relevant coronary stenoses without coronary instrumentation.[11,46] FCA tools use the invasive coronary angiogram or noninvasive computed tomography coronary angiography to estimate FFR-like indices. With both invasive and noninvasive FCA modalities, this is achieved by analyzing data derived from accurate 3-dimensional quantitative coronary angiography with fluid dynamics equations.[46]

Table 1 lists FCA indices that can be measured with commercially available systems. Some FCA tools incorporate patient-specific hemodynamic information, such as Thrombolysis in Myocardial Infarction frame count or aortic pressure at the time the angiogram was obtained in their calculations, allowing a better depiction of boundary conditions. An important aspect of all FCA modalities is that they render physiological longitudinal vessel analysis. Because this is displayed along the angiogram from which it is derived, identification of flow-limiting lesions within the coronary anatomy is readily feasible.[46]

The main characteristics of commercially available FCA systems differ in terms of technical requirements and scientific evidence supporting their therapeutic yield and clinical value.[46] Overall, all have demonstrated good correlation with invasive FFR measurements. For the time being, quantitative flow ratio is the only index that, in addition to showing a high diagnostic yield in studies using invasive FFR as a reference,[47,48] has been compared with angiography to decide coronary revascularization. In a randomized clinical trial, use of quantitative flow ratio was shown to improve 1-year clinical outcomes, compared with angiography.[49] A recent study comparing 5 different FCA systems, using invasive FFR as a comparator, reported a similar diagnostic yield, although the reported areas under the curve were lower than in the independent studies used for validation of each system.[50]

All the above steps in contemporary planning and guidance of PCI using intracoronary pressure guide wires have been explored with FCA, showing the feasibility of identifying diffuse and focal hemodynamic vessel phenotypes,[32] prediction of functional PCI results,[51,52] and presence of residual flow-limiting disease after PCI.[53]

Structured approach to the use of physiology tools in PCI

Figure 4 provides a tentative algorithm integrating the outlined use of wire- and angiography-based physiology tools to plan, guide, and optimize PCI. The algorithm leverages the complementarity of both approaches. For example, angiography-based tools can be used for planning PCI in those cases for which computed tomography coronary angiography or previous invasive angiograms are available. However, they may not be applicable for optimizing PCI when contrast administration must be restricted due to coexisting renal dysfunction, or in long PCI procedures, a context in which wire-based physiology can be used safely.

Final remarks

We believe we are currently entering a new era in the way in which coronary physiology tools will lead to better selection of patients for whom effective treatment of ischemia-generating epicardial disease with PCI can be performed and to guide the interventions to achieve that goal. This may potentially lead to a lower long-term incidence of ischemia-related symptoms and events.

Declaration of competing interest

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Ethics statement and patient consent

This manuscript does not report on patients or patient data.

Supplementary material

To access the supplementary material accompanying this article, visit the online version of the *Journal of the Society for Cardiovascular Angiography & Interventions* at 10.1016/j.jscai.2024.102198.

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