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ASIAN CARDIOVASCULAR LANDSCAPE

Physiology Versus Imaging-Guided Revascularization

Where Are We in 2023?

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Coronary physiological assessment and plaque imaging can provide incremental diagnostic and prognostic information on coronary artery disease (CAD) over that provided by coronary angiography. Physiological assessment can guide treatment decision making by identifying ischemia-causing lesions, while coronary imaging provides detailed morphologic information before and after revascularization. Although these 2 methods have distinct roles, recent clinical data have revealed their similarities and differences under the scope of patient vulnerability (**Figure 1**). In this Asian Cardiovascular Landscape, we aim to cover the pathophysiological concept, current data for the efficacy of physiological vs imaging guidance in treatment decision making and stent optimization, and future directions for the optimal management of patients with CAD.

PHYSIOLOGICAL ASSESSMENT AND IMAGING: CURRENT STATUS

Myocardial ischemia has served as a prerequisite for revascularization in patients with CAD. The current guidelines recommend the use of fractional flow reserve (FFR) or nonhyperemic pressure ratio (NHPR) for treatment decision making, particularly for lesions with angiographically intermediate stenosis. Image-based physiological indexes such as computed tomographic (CT) angiography-derived FFR and angiography-derived FFR can also be used for the identification of functionally significant lesions. The extent and severity of CAD can be assessed using imaging modalities such as intravascular ultrasound (IVUS), optical coherence tomography (OCT), or coronary CT angiography. These modalities can detect certain features of plaque prone to future clinical events by measuring cap thickness, lipid amount, luminal area, plaque burden, and plaque characteristics. As intravascular imaging modalities can directly visualize the lumen in and out of the stent segment as well as stent-related complications, these tools are very helpful in percutaneous coronary intervention (PCI) planning and optimization.

Considering that coronary physiology and imaging assess different aspects of CAD, the use of both may provide the best information on target lesions and selection of the optimal treatment strategy, but their clinical use is still low. Although there are limited epidemiologic data on the use of invasive physiological tests or intravascular coronary imaging in Asian regions compared with Europe and the United States, several studies have demonstrated low penetration of these techniques in Asian countries among patients undergoing PCI.[1] Given the regional variance in medical resources and practice patterns for managing CAD among Asian countries, understanding the similarities and differences in coronary physiology and imaging modalities is crucial for their appropriate application in varying medical environments.

PHYSIOLOGICAL ASSESSMENT AND IMAGING IN DECISION MAKING FOR PCI

Although physiological index-guided treatment decision making is the standard approach, clinical events still occur in deferred patients with FFR > 0.80. High-risk features on imaging modalities are

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ABBREVIATIONS AND ACRONYMS

CAD = coronary artery disease

CT = computed tomographic

FFR = fractional flow reserve

IVUS = intravascular ultrasound

MLA = minimal luminal area

NHPR = nonhyperemic pressure ratio

OCT = optical coherence tomography

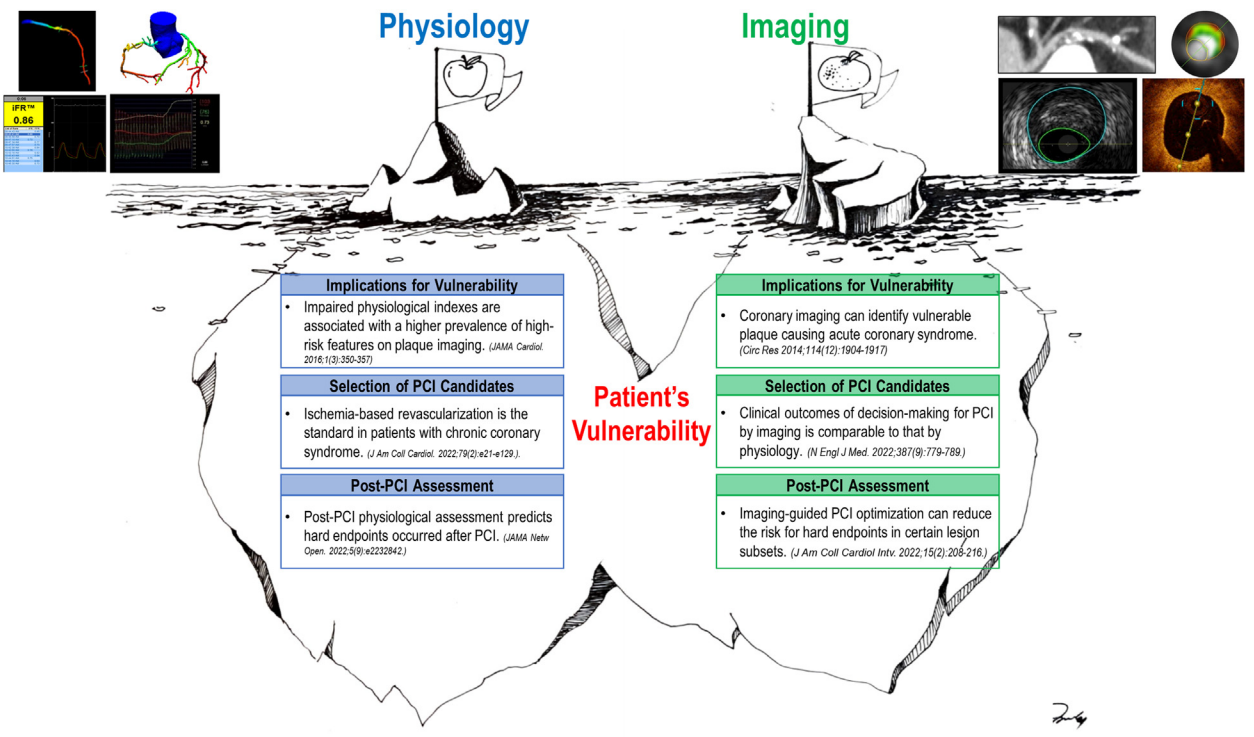
PCI = percutaneous coronary intervention

associated with the risk for clinical events in deferred lesions on the basis of FFR, which supports the prognostic value of imaging parameters independent of physiology. In a post hoc analysis of the CCTA-FFR Registry for Risk Prediction,[2] lesions with FFR ≤0.80 had a 2 to 3 times higher risk for clinical events than lesions with FFR >0.80 under medical treatment, while stented lesions with FFR ≤0.80 showed an attenuated risk. This association was identical in the same population for lesions with plaque burden ≥70% and minimal luminal area (MLA) ≤4 mm^2 (Figure 2). This similarity observed from the hypothesis-generating data might be explained in part by the underlying interplay between hemodynamic status and atherosclerosis. Plaque generally develops at the site of low shear stress, and the progression of atherosclerosis, in turn, alters local hemodynamic environments around the plaque, leading to impaired FFR or NHPR. This increases the mechanical stress acting on the plaque and promotes plaque progression and vulnerable transformation.[3] Previous studies showed that physiological and imaging parameters can represent each other to some extent, and abnormal physiological indexes indicate a higher probability of plaque vulnerability assessed by imaging modalities and vice versa. This continuous interaction provides the pathophysiological base for the similarity between the 2 modalities. It is interesting to note that there may be criteria that warrant a low risk for clinical events after deferral of PCI on the basis of physiological or imaging assessment alone. Although definitive cutoff values need to be elucidated in future studies, the minimum plaque burden that caused an adverse event was 56.2% in the PROSPECT II study,[4] and the prognostic impact of coronary CT angiography–derived plaque features was attenuated in lesions with FFR >0.90.[5]

ROLE OF PHYSIOLOGY AND IMAGING IN PCI OPTIMIZATION

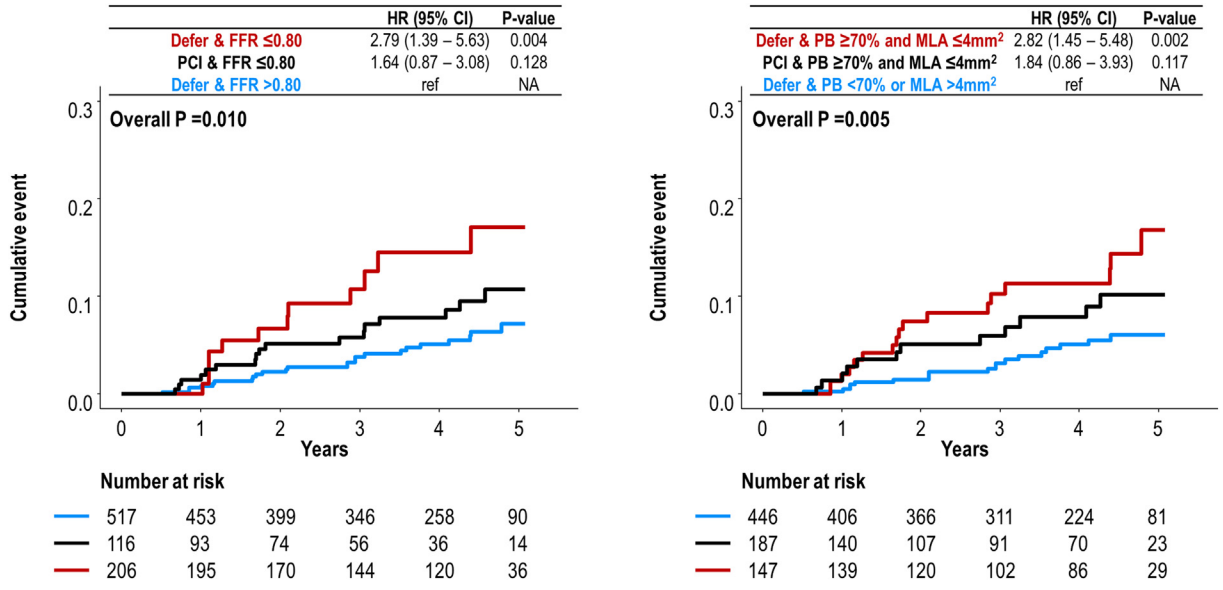
Given that stented lesions, as well as deferred lesions, collectively determine the prognosis of patients with

FIGURE 1 Underlying Concept of Physiology- vs Imaging-Guided Revascularization



Although coronary physiology and imaging provide different aspects of information on coronary artery disease, their fundamental goal in risk stratification and treatment selection is identically based on the patient's vulnerability. PCI = percutaneous coronary intervention.

FIGURE 2 **Outcome Discrimination by Physiology, Imaging, and Treatment Types**



In the CCTA-FFR Registry for Risk Prediction, physiology and imaging parameters could similarly discriminate the clinical outcomes. FFR = fractional flow reserve; MLA = minimum luminal area; NA = not applicable; PB = plaque burden; PCI = percutaneous coronary intervention; ref = reference.

CAD, it is essential to understand how to use coronary imaging and physiology to optimize PCI results. Compared with stent implantation with angiographic guidance, OCT-guided PCI showed a lower rate of malapposed struts and a higher postprocedural FFR, whereas IVUS-guided PCI was associated with a lower risk for major cardiovascular events, especially in patients with complex lesions.

Physiological evaluation also has prognostic implications after stent implantation. In a recent patient-level pooled meta-analysis, a lower post-PCI FFR was associated with a higher risk for 2-year target vessel failure or cardiac death or myocardial infarction.[6] However, the benefit of physiological index-guided stent optimization still needs further investigation, as a post-PCI FFR-guided optimization strategy failed to increase the proportion of FFR ≥0.90 or to reduce target vessel failure at 1-year follow-up in recent studies.[7] Therefore, although post-PCI physiological indexes can be used as prognostic markers, their role as a procedural endpoint to improve clinical outcomes needs more data. Ongoing studies will test the efficacy of the assessment of functional or physiological CAD patterns by pressure wire pull back for the procedural planning and selection of appropriate PCI targets.[7]

PHYSIOLOGY- VS IMAGING-GUIDED PCI: HEAD-TO-HEAD COMPARISON

Several studies have directly compared between physiology-guided vs imaging-guided treatment in terms of clinical outcomes to shed light on the effective way to assess and treat patients with CAD. In a network meta-analysis, no differences were observed between FFR-guided or IVUS- and/or OCT-guided PCI in reducing a composite of death or myocardial infarction or revascularization.[8] In the FORZA (FFR or OCT Guidance to Revascularize Intermediate Coronary Stenosis Using Angioplasty) trial, with 350 patients with intermediate lesions randomized 1:1 to OCT-guided PCI (ie, PCI if OCT-derived lumen area stenosis ≥75% or 50% < area stenosis <75% with MLA <2.5 mm^2, or plaque rupture) vs FFR-guided PCI, the rate of target vessel failure at 13 months was lower in the OCT group (7.4% vs 2.3%; $P = 0.027$), while the rate of medical management was higher and total cost was lower in the FFR group.[9] A recent randomized controlled trial, the FLAVOUR (Fractional Flow Reserve and IVUS for Clinical Outcomes in Patients With Intermediate Stenosis) study, compared IVUS-guided PCI (ie, PCI performed if MLA ≤3 mm^2 or 3 mm^2 < MLA ≤4 mm^2

with plaque burden ≥70%) and FFR-guided PCI strategies in 1,682 patients with intermediate stenosis. The rates of a composite of death, myocardial infarction, or revascularization at 24 months were 8.1% and 8.5% in the FFR and IVUS groups, respectively ($P = 0.01$ for noninferiority), and the rate of PCI was lower in the FFR group.[10] Although more data are needed to reach a decisive conclusion, current evidence indicates that image- and physiology-guided PCI can provide comparable clinical outcomes with a lower PCI rate with physiological assessment. However, whether this finding is driven by their impact on decision making for PCI, PCI optimization, or both still needs further investigation, as each study used different imaging criteria for PCI. In addition, PCI optimization was performed on the basis of post-PCI imaging or FFR criteria in both FORZA and FLAVOUR, whereas a network meta-analysis included all studies in which IVUS, OCT, or FFR was used for either decision making or PCI optimization.

FUTURE PERSPECTIVES

Ongoing studies are expected to further unveil the prognostic implications of imaging and physiological assessments. Relative implications between imaging- and physiology-guided PCI will be investigated, such as OCT-guided VS FFR- or NHPR-guided treatment in the INTERCLIMA (Interventional Strategy for Non-Culprit Lesions With Major Vulnerability Criteria at OCT in Patients With ACS; NCT05027984) or quantitative flow ratio-guided vs IVUS-guided treatment in the FLAVOUR II (Angiography-Derived FFR and IVUS for Clinical Outcomes in Patients With Coronary Artery Disease; NCT04397211). As for the integrative approach with imaging and physiology, the PREVENT (Preventive PCI or Medical Therapy Alone for Vulnerable Atherosclerotic Coronary Plaque; NCT02316886) will show whether PCI for a vulnerable plaque with FFR >0.80 can improve clinical outcomes. The efficacy of selective PCI for lesions with both FFR ≤0.75 and OCT-defined vulnerable features will be compared with that of PCI for all lesions with FFR ≤0.80 in the COMIBINE-INTERVENE (Combined Ischemia and Vulnerable Plaque Percutaneous Intervention to Reduce Cardiovascular Events; NCT05333068). Clinical trials based on novel physiological approaches such as imaging-based physiological indexes, longitudinal vessel analysis using pull back pressure gradients, or synchronized instantaneous wave-free ratio pull back with coronary angiogram (NCT04451044) will show the effectiveness of physiology-based PCI planning. Throughout all these explorations, we will be able to get closer to our goal of optimal decision making and treatment for patients with CAD through the appropriate and integrative use of imaging and physiology data.

CONCLUSIONS

Coronary physiological and imaging modalities are useful in selecting patients for revascularization and PCI optimization. The pathophysiological interplay between hemodynamic status and plaque can explain the similarity in outcome discrimination between the 2 modalities. More studies are needed to further reveal the appropriate treatment strategies for lesions with discordance between functional significance and plaque features to provide the effective individual approach with physiology and imaging in patients with CAD.

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