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EDITORIAL COMMENT

Coronary Physiology Assessment

On Becoming Faster, Friendlier, and a Better Guiding Companion*

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Physiologic assessment of coronary artery disease plays a crucial role in guiding the decision to proceed with percutaneous coronary intervention (PCI), bypass surgery, or revascularization deferment. The validity of coronary physiology assessment and superior clinical outcomes with physiology-guided PCI compared with angiography-guided PCI have been reasonably established by randomized trials.[1,2] With many recent advancements as well as emerging modalities in this field, comprehensive consideration and clinical practice guidance are warranted.

In this issue of *JACC: Asia*, Koo et al[3,4] provide such a timely and focused comprehensive evidence-based 2-part report on the practical application of coronary physiology assessment. Consensus statements regarding coronary physiology have been published from organizations in other continents, one from the European Association of Percutaneous Cardiovascular Interventions (EAPCI) of the European Society of Cardiology[5] and another from the Society of Cardiac Angiography and Interventions (SCAI).[6] The Koo et al[3,4] report is unique with its thoroughness and particular attention to incorporating studies from the Asia-Pacific region.

As meticulously documented in the articles, there are abundant data to support the validity of coronary physiology to guide the revascularization decision-making process. What is needed, and is steadily being provided, are strategies to make the technologies of assessing coronary physiology more friendly companions to busy catheterization laboratory practice. Simply put, there are multiple studies showing superior clinical outcomes with physiology-guided interventions compared with angiography-guided ones, but utilization remains limited. Coronary physiology assessment is given Class I recommendation for angiographically intermediate stenoses by the current guidelines.[7,8] Except for culprit lesions in acute coronary syndromes and angiographically severe (ie, unequivocally significant) lesions, the functional relevance of coronary artery narrowings should be investigated before interventions with the use of either noninvasive or invasive modalities. Surprisingly, despite this truism, the use of invasive coronary physiology among all PCI cases remains remarkably low (5%-10%) in Asian countries as well as in Europe and North America, suggesting that angiography-guided PCI without physiologic (noninvasive or invasive) assessment is the practice norm.[9,10] There are many reported reasons for the current underutilization of coronary physiology assessment, including its cost or lack of reimbursement, longer procedural times, uncertainty of case-specific benefit, possible complications, and long-standing reliance on visual assessment alone.

There are several ways to incorporate coronary physiology in a pre-interventional setting, such as pre-procedural coronary computed tomography-derived fractional flow reserve (CT-FFR). The PRECISE trial showed that a strategy utilizing CT-FFR for the evaluation of patients with stable chest pain led to a lower rate of "catheterization without obstructive disease" with similar safety outcomes compared with usual testing.[11] In the procedural setting, there are ways to address the time factor and complications, such as the use of nonhyperemic pressure ratios (eg, instantaneous wave-free ratio) which removes

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the need for an infusion of a coronary vasodilator to achieve maximal hyperemia and leads to fewer side-effects and shorter procedural time.[12] Together, more liberal use of noninvasive or invasive coronary physiology assessments should provide a decrease in unwarranted invasive coronary angiograms or PCI procedures without an increase in safety concerns. Regarding the cost-effectiveness of physiology-guided revascularization, FFR-guided PCI may result in an overall lower cost than angiography-guided PCI via a reduction in index-procedure stents and subsequent adverse events, thereby offsetting the initial cost of physiology assessment.[13]

Another way to augment the utilization of coronary physiology is by making it simpler, friendlier, and potentially automated. Examples include the evolution and adoption of angiography-derived invasive coronary physiology assessment, such as virtual FFR (vFFR) or quantitative flow ratio (QFR), into routine practice. The FAVOR III China trial showed the superiority of QFR-guided PCI compared with angiography-guided PCI, driven by a significant reduction in myocardial infarction.[14] This observed benefit of reduction of myocardial infarction (primarily reduction of periprocedural infarctions) is similar to what was observed in the FAME trial, which compared wire-based, FFR-guided PCI vs angiography-guided PCI.[2] QFR could potentially eliminate some of the issues of invasive wire-based coronary physiology, such as cost of equipment, procedure time, and possible complications. The ongoing FAVOR III Europe Japan trial (NCT03729739) is anticipated to provide further supporting evidence of this promising modality. Looking further forward, it is very easy to imagine the routine use of machine learning combined with vFFR or QFR in the catheterization laboratory to establish the real-time need for PCI and assess the quality of the revascularization.

This leads us to an ongoing knowledge gap or area without certain proof—whether coronary physiology can be used after PCI to "dial in" or optimize final PCI results and meaningfully affect subsequent clinical outcomes. The general association between lower post-PCI coronary physiology indices and higher subsequent ischemic events is established.[15] Yet, the clinical benefit of prospectively targeting a specific FFR, instantaneous wave-free ratio (iFR), or QFR goal during PCI remains uncertain. The ongoing DEFINE GPS trial (NCT04451044), which targets a post-PCI iFR ≥0.95, is trying to address this important question.

Intracoronary imaging and coronary physiology are distinct ways to evaluate coronary anatomy and physiology, respectively. The utility of intracoronary imaging such as intravascular ultrasound (IVUS) as a substitute for coronary physiology assessment to guide revascularization decisions is a relevant clinical question, especially in Asian countries where the use of intracoronary imaging is particularly high. The FLAVOUR trial randomized patients with intermediate stenosis to either an FFR-guided or an IVUS-guided procedure.[16] Of note, IVUS was used to determine whether to perform PCI in addition to optimizing PCI results in the IVUS group. The primary ischemic event rate was similar between the groups, but the IVUS-guided group had a significantly higher rate of index PCI than the FFR-guided group (65% vs 44%). Thus, a physiology-guided strategy (such as FFR or iFR) remains the standard invasive measure to guide the revascularization indication. That being said, intracoronary imaging and coronary physiology complement each other and together provide more complete information. Hybrid modality-guided PCI with intracoronary imaging and coronary physiology may further improve the outcomes of coronary artery disease. With this thinking, the potential benefits of PCI in physiologically nonsignificant lesions with anatomically high-risk features, such as large plaque burden, are currently being tested in a randomized fashion in the PREVENT trial (NCT02316886).

In summary, the Asia-Pacific Expert Consensus Document regarding coronary physiology is a useful clinical practice guide for physicians not only in Asian-Pacific countries but also for physicians worldwide. Many ongoing trials and industry-related efforts are expected to lead to further refinements in coronary physiology assessment and improve its adoption and utilization into clinical practice, so that these companions will be more frequently invited to our gatherings.

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