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COMMENTARY

The Importance of Measuring Coronary Blood Flow for Clinical Decision Making

Cynthia Yeung[1], Adrian Baranchuk[1], Gary Tse[2,3] and Tong Liu[4,*]

[1]*Queen's University, Kingston, Ontario, Canada;* [2]*Department of Medicine and Therapeutics, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong, China;* [3]*Li Ka Shing Institute of Health Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong, China;* [4]*Department of Cardiology, Tianjin Institute of Cardiology, Second Hospital of Tianjin Medical University, Tianjin, China*

TO THE EDITOR

The assessment of coronary blood flow is of paramount importance in terms of determining the effectiveness of a coronary revascularization procedure and ultimately, the restoration of myocardial perfusion. Coronary microcirculation cannot be directly visualized in the catheterization laboratory, and angiography cannot assess the extent to which a coronary stenosis contributes to myocardial ischemia [1]. Therefore, functional and surrogate measures for quantifying coronary physiology are crucial adjuncts for clinical decision making.

We read with interest the review by Vijayan, *et al.* [2] on the assessment of coronary blood flow physiology in the cardiac catheterization laboratory [2]. This paper covers the major surrogate measures of coronary physiology, as well as the invasive and non-invasive methods of coronary flow quantification. Their review of the current literature on coronary blood flow is important because absolute coronary blood flow measurements are valuable for risk stratification, assessing prognosis, and monitoring the effectiveness of risk reduction strategies [3, 4]. Moreover, myocardial blood flow physiology is dependent on a complex interplay of factors, including the patency of the epicardial vessels, autoregulation of coronary vascular tone, perfusion pressures, and luminal obstructions [5]. Therefore, the accurate evaluation of flow impairment not attributable to coronary artery disease and less obvious microvascular obstructions help develop a better understanding of pathological processes [3, 6].

Coronary blood flow physiology in humans was originally investigated by Knoebel, *et al.* in 1972, [7] and popularized by the work of Gould, *et al.* on coronary flow reserve and resistance [8]. Notably, Vijayan, *et al.* [2] highlighted the advantages, disadvantages, and limitations of each approach to assessing coronary blood flow. Their analysis of the nuanced differences between the indices lends to an informed discussion on the subsequent implications for clinical practice. For example, the authors explain how the relative contribution of epicardial stenosis and microvascular disease can be elucidated when the surrogate measures of coronary blood flow physiology are considered in combination. Overall, the paper provides a thorough evaluation of the current approaches for assessing coronary blood flow in the catheterization laboratory.

However, we notice that the emphasis is heavily biased towards the validity of each measurement in terms of theoretical representation of the actual blood flow, and that Vijayan, *et al.* only briefly considered patient-centered factors in the assessment of coronary blood flow. The suitability of a measure for coronary blood flow lies not only in the value of the diagnostic information it provides, but also in the associated impact of obtaining that information. For example, the attractiveness of avoiding complications involved with the administration of adenosine has motivated research on vasodilator-free indices. Gotberg, *et al.* introduced Instantaneous Wave-free Ratio (iFR) as an alternative to Fractional Flow Reserve (FFR) that does not require the induction of hyperemia [9]. However, the authors did not mention other non-hyperemic indices, such as resting distal to aortic coronary pressure (P_d/P_a) and Resting Full-cycle Ratio (RFR). Unlike iFR, resting P_d/P_a is a whole-cycle measurement not limited to the wave-free diastolic period. P_d/P_a shows excellent agreement with iFR and may be analyzable in a higher proportion of patients than iFR [10, 11]. Moreover, diagnostic accuracy can be improved with the use of both the iFR and P_d/P_a [12]. A pooled analysis by Maini, *et al.* reported that P_d/P_a shows adequate agreement with FFR for coronary stenosis severity [13]. A related index, RFR, is diagnostically equivalent to iFR, but leverages its unbiased detection of the lowest P_d/P_a during the full cardiac cycle to potentially unmask physiologically significant coronary stenoses that would otherwise be missed by assessment dedicated to specific segments of the cardiac cycle [14]. Given the side effects related to adenosine and other pharmacological agents, a comprehensive overview of vasodilator-free indices of coronary blood flow should be incorporated into their impressive review.

Similarly, the impact of catheter insertion on the coronary arteries is another topic not explored by Vijayan, *et al.*

*Address ccorrespondence to this author at the Department of Cardiology, Tianjin Institute of Cardiology, the Second Hospital of Tianjin Medical University, Tianjin, China; Tel: +86 88328617; Fax: +86 28261158; E-mail: liutongdoc@126.com

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that we believe justifies attention. Excessive catheter manipulation results in the exposure of endothelial cells in the atrium to high wall shear stress and increased platelet aggregation in the blood flow [15]. Thus, novel techniques that quantify coronary blood flow and microvascular resistance in real time and minimize the instrumentation of the coronary arteries are hugely desirable. Virtual resting P_d/P_a is one such technique undergoing preliminary research that utilizes routine angiographic data with a flow model and, unlike P_d/P_a, it does not require a pressure-wire. The high diagnostic performance of virtual resting P_d/P_a for predicting FFR is promising for future implementation in clinical practice [16].

Furthermore, we would like to add to the discussion on non-invasive methods of coronary flow quantification. Waller, *et al.* mentioned the lack of real-time results in positron emission tomography and complex post-processing required for Cardiac Magnetic Resonance (CMR) as barriers for widespread use [4]. However, the field is developing more time-efficient protocols that may help the translation of these technologies to more ubiquitous application [17]. Moreover, recent innovations on CMR fluoroscopy catheterization are also overcoming other obstacles. For example, the use of commercial nitinol guidewire in combination with low specific absorption rate imaging from gradient echo spiral acquisitions circumvents the commercial metallic guidewires, which have been considered contraindicated due to concerns about radiofrequency-induced heating [18]. The non-invasive methods of coronary flow quantification demonstrate the potential for more universal use as they continue to be more refined.

Vijayan, *et al.* [2] should be congratulated for their efforts in elegantly summarizing the complex topic of coronary blood flow assessment that will help physicians and specialists to apply a combination of these indices tailored to individual patients for clinical decision making. Their review also stimulates research on the development of novel tools for absolute coronary blood flow measurements in the catheterization laboratory, and highlights the importance of validating new techniques in larger series for the improvement of patient outcomes.

LIST OF ABBREVIATIONS

CMR	=	Cardiac Magnetic Resonance
P_d/P_a	=	Distal to Aortic Coronary Pressure
FFR	=	Fractional Flow Reserve
iFR	=	Instantaneous wave-Free Ratio
RFR	=	Resting Full-cycle Ratio

CONSENT FOR PUBLICATION

All authors have participated in the work and have reviewed and agree with the content of the article.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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