The Importance of Measuring Coronary Blood Flow for Clinical Decision Making

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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 (Pd/Pa) and Resting Full-cycle Ratio (RFR). Unlike iFR, resting Pd/Pa is a whole-cycle measurement not limited to the wave-free diastolic period. Pd/Pa 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 Pd/Pa [12]. A pooled analysis by Maini, et al. reported that Pd/Pa 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 Pd/Pa 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.
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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REFERENCES

[1] White CW, Wright CB, Doty DB, et al. Does visual interpretation of the coronary arteriogram predict the physiologic importance of a coronary stenosis? N Engl J Med 1984; 310(13): 819-24.
[2] Vijayan S, Barmby DS, Pearson IR, Davies AG, Wheatcroft SB, Sivanathan M. Assessing coronary blood flow physiology in the cardiac catheterisation laboratory. Curr Cardiol Rev 2017; 13(3): 232-43.
[3] van de Hoef TP, Siebes M, Spaan JA, Pick J. Fundamentals in clinical coronary physiology: why coronary flow is more important than coronary pressure. Eur Heart J 2015; 36(47): 3312-9a.
[4] Waller AH, Blankstein R, Kwong RY, Di Carli MF. Myocardial blood flow quantification for evaluation of coronary artery disease by positron emission tomography, cardiac magnetic resonance imaging, and computed tomography. Curr Cardiol Rep 2014; 16(5): 483.
[5] van de Hoef TP, Nolte F, Rolandi MC, et al. Coronary pressure-flow relations as basis for the understanding of coronary physiology. J Mol Cell Cardiol 2012; 52(4): 786-93.
[6] Wu KC, Zerhouni EA, Judd RM, et al. Prognostic significance of microvascular obstruction by magnetic resonance imaging in patients with acute myocardial infarction. Circulation 1998; 97(8): 765-72.
[7] Knoebel SB, McHenry PL, Phillips JF, Pauletto FJ. Coronary collateral circulation and myocardial blood flow reserve. Circulation 1972; 46(1): 84-94.
[8] Gould KL, Lipscomb K. Effects of coronary stenoses on coronary flow reserve and resistance. Am J Cardiol 1974; 34(1): 48-55.
[9] Gotberg M, Christiansen EH, Gudmundsdottir IJ, et al. Instantaneous wave-free ratio versus fractional flow reserve to guide PCI. N Engl J Med 2017; 376(19): 1813-23.
[10] Kobayashi Y, Johnson NP, Zimmermann FM, et al. Agreement of the resting distal to aortic coronary pressure with the instantaneous wave-free ratio. J Am Coll Cardiol 2017; 70(17): 2105-13.
[11] Lee JM, Park J, Hwang D, et al. Similarity and difference of resting distal to aortic coronary pressure and instantaneous wave-free ratio. J Am Coll Cardiol 2017; 70(17): 2114-23.
[12] Shiode N, Okimoto T, Tamekiiyo H, et al. A comparison between the instantaneous wave-free ratio and resting distal coronary artery pressure/aortic pressure and the fractional flow reserve: The diagnostic accuracy can be improved by the use of both indices. Intern Med 2017; 56(7): 749-53.
[13] Maini R, Moscona J, Sidhu G, et al. Pooled diagnostic accuracy of resting distal to aortic coronary pressure referenced to fractional flow reserve: The importance of resting coronary physiology. J Interv Cardiol 2018; 31(5): 588-98.
[14] Svanerud J, Ahn JM, Jeremias A, et al. Validation of a novel non-hyperemic index of coronary artery stenosis severity: The Resting Full-cycle Ratio (VALIDATE RFR) study. EuroIntervention 2018; 14(7): 806-14.
[15] Tian X, Sun A, Liu X, et al. Influence of catheter insertion on the hemodynamic environment in coronary arteries. Med Eng Phys 2016; 38(9): 946-51.
[16] Papafilis ML, Muramatsu T, Ishibashi Y, et al. Virtual resting $P_d/P_a$ from coronary angiography and blood flow modelling: Diagnostic performance against fractional flow reserve. Heart Lung Circ 2018; 27(3): 377-80.
[17] Tsj O, Rjg K, Jh C, M W, Fm VZ. Myocardial blood flow and myocardial flow reserve values in (13)N-ammonia myocardial perfusion PET/CT using a time-efficient protocol in patients without coronary artery disease. Eur J Hybrid Imaging 2018; 2(1): 11.
[18] Campbell-Washburn AE, Rogers T, Stine AM, et al. Right heart catheterization using metallic guidewires and low SAR cardiovascular magnetic resonance fluoroscopy at 1.5 Tesla: first in human experience. J Cardiovasc Magn Reson 2018; 20(1): 41.