Resting Indices of Coronary Lesion Severity
Not Always as Simple as It Seems

Martijn A. van Lavieren, MSc; Jan J. Piek, MD, PhD

Physiological guided percutaneous coronary intervention (PCI) has been demonstrated to result in a better clinical outcome compared with angiographic guidance alone.1 Pressure and Doppler-tipped guide wires that can be used for intracoronary physiological assessment were introduced >2 decades ago. Fractional flow reserve (FFR) has emerged as the most widely used physiological index in current clinical practice. This pressure-only index estimates the functional significance of a coronary stenosis by quantifying the trans-stenotic pressure ratio under hyperemic conditions2 and has been well validated throughout the years.3 However, the prerequisite of inducing stable hyperemia is considered the main practical limitation of FFR measurements that has hampered its embedment in clinical practice.

More recently, nonhyperemic pressure-derived indices were introduced to accommodate the need to further simplify physiological assessment; instantaneous wave-free ratio (iFR) and whole-cycle distal to proximal pressure ratio (Pd/Pa). Both indices make use of a trans-stenotic pressure gradient across a stenosis during resting conditions, obtained with conventional pressure wires and, in case of iFR, appropriate software. iFR assesses the pressure ratio in a particular part of the diastole, the wave-free period, where microvascular resistance is constant and minimal.4 Thereby, it relies on the same theoretical framework as FFR. Both iFR and whole-cycle Pd/Pa are shown to have equivalent diagnostic accuracy for the detection of ischemia-generating coronary stenoses when compared with FFR.5

These nonhyperemic pressure-derived indices rely on smaller differences in trans-stenotic pressure than FFR and are thereby more vulnerable to technical and procedural errors affecting distal and aortic pressure. These errors result in pressure drift that in general becomes overt at the end of the procedure when equality of signals is verified again with the pressure sensor located just inside the guiding catheter. Drift can be observed as an absolute or relative pressure offset between both signals, which can originate from drift of the pressure wire sensor and changes in aortic pressure. It may cause stenosis misclassification, especially when indices values are close to their cutoff values.

In this issue of Circulation: Cardiovascular Interventions, Cook et al6 report a single-center study in which they quantify the effect of clinically tolerated levels of pressure wire drift on the rates of reclassification with FFR, iFR, and whole-cycle Pd/Pa. They enrolled 447 patients (447 stenoses) who underwent physiological stenosis severity assessments and conducted the measurements in a robust and standardized fashion, that is, by fixing the aortic pressure transducer and eliminating coronary artery spasm by the administration of 300 µg nitroglycerine before the procedure. Aortic and distal pressures were recorded during resting condition and stable hyperemia, using intravenous or intracoronary administration routes for adenosine. At the end of the procedure, pressure drift was checked, and if found to be >2 mmHg, the entire recording was repeated. All data were analyzed off-line, and both aortic and wire pressure drifts were assessed, offsetting the pressure trace relative to its original position by 1-mm Hg increments from −2 to +2 mm Hg. FFR, iFR, and Pd/Pa were recalculated for different origins and degrees of pressure drift.

The present study shows that a pressure wire drift of ±2 mm Hg causes stenosis misclassification in all contemporary-used pressure-derived indices, in particular when close to the cutoff value. The effect of drift originating from changes in distal pressure resulted in reclassification in 21%, 25%, and 33% with FFR, iFR, and whole-cycle Pd/Pa, respectively. Both FFR and iFR had significantly lower proportions of misclassification than Pd/Pa. The effect of pressure drift originating from aortic pressure drift yielded similar results. FFR and iFR are reported to be less susceptible to drift than whole-cycle Pd/Pa. The authors further conclude that measurements need to be repeated when drift exceeds ±2 mm Hg.

The present study is the first to assess the impact of drift on stenosis misclassification in a systematic way. The authors address a relevant and important topic of the influence of pressure drift on the sensor-equipped guide wires on the assessment and classification of functional stenosis severity by pressure-only-derived indices. The present study is of particular interest in an era where physiological stenosis severity assessment is shifting toward nonhyperemic indices. Several thresholds for pressure drift are proposed and used in core laboratory analyses.7,8 Core laboratories apply a threshold of ±2 mm Hg, although the present study shows that it already causes severe reclassification. Unfortunately, data on the influence of pressure drift on physiological indices are lacking, and the present study provides valuable insight into a phenomenon frequently encountered by those performing these physiological measurements in clinical practice.
The pressure wire is not always the source of error. Pressure drift can originate from many other sources as presented by Cook et al. in Table 1 of their article. Cook et al. performed their measurements in a robust methodological fashion, thereby eliminating the likelihood of drift induced on the aortic pressure signal and mainly focused on the drift originating from the pressure wire. However, it is this drift on the aortic pressure signal that, because of procedural errors, should be considered the main source of the observed drift. In particular, the alteration of the pressure transducer height after normalization and not removing the needle guidewire introducer are frequently encountered errors during physiological assessment that affect the aortic pressure signal. With the introduction of nonfixed aortic pressure transducers lying loosely on top of the patient, shifting the transducer by only 3 cm in height, a pressure drift as high as 2 mmHg is induced originating from the aortic pressure rather than from the pressure wire sensor. However, these rather small procedural errors are often not noticed.

Pressure drift is often depicted as the absolute difference between aortic and distal pressure but can also be assessed as a ratio. The impact of absolute pressure drift on stenosis classification may differ depending on the absolute values of mean aortic pressure. For example, in a patient with a mean arterial pressure of 120 mmHg, the relative influence of a pressure drift of 5 mmHg, according to the expert consensus, is less than that of a patient with a mean arterial pressure of 90 mmHg. This effect is of particular interest when hyperemia is induced by means of continuous administration of intravenous adenosine, where often a pronounced decrease in arterial pressure is observed due to systemic vasodilation. It could be postulated that assessing the relative pressure drift is preferred to assessing an absolute drift to accommodate the relative impact of drift on the physiological measurements depending on the mean arterial pressure.

Despite the fact that the ±2 mmHg threshold for clinically accepted drift is used in core laboratory analyses of numerous studies, the threshold for drift itself has never been a subject of extensive research. The proposed thresholds of clinically acceptable drift range widely. The present study underscores the importance of adhering to the stringent threshold also used in core laboratory analysis. This is of particular importance when the indices are close to the cutoff value, ±0.05 U of their cutoff value, in which the authors report that for iFR and whole-cycle Pd/Pa reclassification occurred in 50.1% and 62.1%, respectively. This indicates that drift cannot be tolerated using nonhyperemic indices that are close to the cutoff value and the ±2 mmHg might already be too liberal. On the contrary, when values are far away from their cutoff value, drift is unlikely to result in stenosis misclassification.

Evidence for the usefulness of nonhyperemic indices, such as iFR and whole-cycle Pd/Pa, for the assessment of physiological stenosis severity is accumulating. It is conceivable that these indices, because of their ease of use, will be more frequently applied in daily clinical practice. However, the use of resting indices for the evaluation of coronary stenosis severity is not always as simple as it seems. They are more vulnerable for drift, resulting in a marked and clinically significant misclassification, in particular when indices are close to their cutoff value. Physiological assessment should always be performed in a careful and meticulous manner to avoid procedural and technical sources of drift and ensure optimal conditions for clinical decision making.

Disclosures
M.A. van Lavieren and Dr Piek have served as speakers at educational events organized by Philips Volcano Corporation.

References
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