

Utility of the pressure guidewire in diabetic patients

Utilidad de la guía de presión en pacientes diabéticos

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Blood pressure indices like fractional flow reserve (FFR) and the instantaneous wave-free ratio (iFR) measure the distal-to-aortic pressure ratio of a lesion in a similar way using a pressure guidewire. FFR requires the induction of maximal hyperemia while the iFR is an index based on the assessment of pressure curves at rest. There is solid confirmation of the validity and efficacy of such indices from multiple studies while their use is widely backed by the clinical practice guidelines.¹

However, the efficacy of blood pressure indices is based on 2 fundamental objectives. The first one is to prove that they are useful to indicate the revascularization of a lesion when the resulting value is below the cut-off point (≤ 0.80 for the FFR, and ≤ 0.89 for the iFR). The second one is to demonstrate that lesions with values above the cut-off point (> 0.80 or > 0.89 , respectively) have a low risk of requiring revascularization, and lack of ischemic events at follow-up. Conceptually, the first indication is clear: a lesion with pathological values is an obstructive lesion that causes ischemia now. Therefore, if clinically indicated (and technically feasible) the best thing to do is to revascularize such a lesion. The second indication has a higher degree of uncertainty because a lesion that does not cause ischemia (now) does not necessarily mean that it will not cause it at some point in the future. This is so because the capacity of blood pressure indices (with normal results) to detect vulnerable plaques is limited, and they show a greater tendency towards progression or destabilization. Therefore, the negative predictive value of pressure indices is supposed to be worse when used in patients with a higher risk of progression into atherosclerotic cardiovascular disease.

Proof of this is that recent studies conducted in patients with acute myocardial infarction (AMI) and multivessel disease have demonstrated that the FFR of non-culprit lesions does not provide any clinical benefits regarding the revascularization of such lesions estimated visually and, therefore, under angiographic guidance.^{2,3} The prevalence of vulnerable plaques causing visual stenosis between 50% and 69% in non-culprit vessels of patients with AMI is estimated at around 30%. Actually this rate is probably higher when lesions with a greater degree of angiographic obstruction are studied.⁴ The COMBINE OCT-FFR trial also reported a similar rate of vulnerable

plaques (25%) on the optical coherence tomography performed in diabetic patients with angiographic stenoses between 40% and 80% and normal FFR values.⁵ In this study, angiographic lesions with normal FFR values associated with vulnerable plaques had more adverse events (cardiac death, target vessel myocardial infarction, and clinically driven target lesion revascularization) compared to those not associated with vulnerable plaques (13% vs 3%; $P < .001$).

The article by Castro-Mejía et al.⁶ recently published in *REC: Interventional Cardiology* provides the mid-term follow-up (3.5 years) of a large single-center registry of patients with intermediate angiographic lesions assessed using blood pressure indices and with normal results. This study compared the adverse events between diabetic and nondiabetic patients with the necessary statistical adjustments to compensate for the inherent differences of the baseline characteristics of both groups. The authors conclude that blood pressure indices (FFR and iFR) had a similar efficacy in diabetic and nondiabetic patients for not predicting future target vessel myocardial infarctions or the need for target lesion revascularization. However, we should mention that diabetic patients had higher rates of all-cause mortality, AMI, and need for revascularization compared to nondiabetic patients.⁶ We should specifically mention that there was a 2.6-fold higher risk of infarction in any vessels at the follow-up in diabetic compared to nondiabetic patients ($P < .063$ after adjustments). However, only 13% of the AMIs registered were adjudicated to the study vessel in diabetic vs 38% in nondiabetic patients.⁶ This difference can be due to chance alone or to the fact that the lesions that cause AMIs at the follow-up are scarcely susceptible to be studied with a pressure guidewire at the index procedure in diabetic patients. It is well known that these patients have more diffuse atherosclerotic cardiovascular disease, which complicates the correct angiographic assessment of the lesions (and, also, prevents the use of a pressure guidewire in such vessel for assessment purposes). It is highly likely that a strategy based on intravascular imaging modalities alone or in combination like in the COMBINE OCT-FFR trial can be of greater utility to detect this type of lesions.

Three recent studies have reported contradictory outcomes regarding the negative predictive value of blood pressure indices in diabetic patients. Kennedy et al.⁷ found more AMIs and a greater need for



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target lesion revascularization with normal FFR values in diabetic patients at the 3-year follow-up. On the contrary, Van Belle et al.⁸ found no differences between diabetic and nondiabetic patients who were deferred (for having normal FFR values) in 2 large registries conducted in Portugal, and France at the 1-year follow-up. No significant differences were seen either in the DEFINE-FLAIR substudy that analyzed adverse events between diabetic and nondiabetic patients in deferred patients at 1-year follow-up.⁹ It should be interesting to assess the long-term follow-up of these last 2 studies to see if the negative predictive value of blood pressure indices stays the same in diabetic and nondiabetic patients.

Finally, Castro-Mejía et al.⁶ propose that resting physiological indices with nonpathological findings may have a better negative predictive value compared to the FFR values of diabetic patients. This would be explained by the fact that one of the causes of discrepancy between the FFR and the iFR is microvascular dysfunction (that is more common in diabetic patients). Patients with microvascular dysfunction can have smaller drops of the pressure index during maximal hyperemia since not enough hyperemia is induced. However, resting physiological indices are not hyperemia-dependent, meaning that they should be more sensitive to detect significant epicardial lesions. However, this hypothesis was not confirmed by the DEFINE-FLAIR substudy on deferred diabetic patients.⁹

In conclusion, diabetic patients still remain as one of the challenges of interventional cardiology because they have more adverse events compared to nondiabetic patients (despite the proper optimal medical therapy). A more aggressive strategy to assess intermediate coronary lesions using pressure guidewires is advisable to guide complete revascularization in diabetic patients. Future studies should also assess whether a mixed strategy with intravascular imaging modalities of nonfunctionally significant arteries can be useful to prevent future events in this group of patients.

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