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Editorial

Contrast fractional flow reserve: Attractive alternative to non-hyperaemic pressure ratios for coronary disease evaluation

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Fractional flow reserve (FFR)-guided management improves decision-making and health and economic outcomes in patients with coronary artery disease. Introduced in 1993 by Pijls and De Bruyne, FFR is defined as the ratio of maximal myocardial flow in the stenotic territory to maximal flow in the same territory in the hypothetical case that stenosis is absent. However, FFR requires pharmacological maximal vasodilation, commonly by adenosine, to minimise microvascular resistance, because it relies on the theoretical principle that a linear pressure-flow relationship in the coronary tree may only be presumed if resistance in the coronary tree is constant and minimal. Pharmacological agents to induce maximal hyperaemia can be unpleasant for patients, increase procedure time and related costs, which may lead to underutilisation of FFR in clinical practice.

Non-hyperaemic pressure ratio (NHPR) is the recently established unifying term to encompass the emerging family of resting pressure indices, which effectively have equivalent clinical significance [1]. NHPR, notably the ratio of pressures distal and proximal to a stenosis (Pd/Pa) [2], the instantaneous 'wave free' ratio (iFR) [3], the resting full-cycle ratio (RFR) [4] and the diastolic pressure ratio (dPR) [1] have been proposed as alternative options to conventional FFR for assessing functional lesion significance. In the RESOLVE pooled analysis, the diagnostic accuracy of either Pd/Pa or iFR in predicting an ischaemic FFR was 80% [5]. However, for iFR and resting Pd/Pa values in the equivocal 'grey zone', where predictive value for ischaemic FFR is lowest, a hybrid approach with adenosine was suggested.

Another approach for assessing the functional significance of a coronary stenosis is contrast FFR (cFFR), which exploits the property of radiographic contrast to induce submaximal hyperaemia [6]. Attractive through its simplicity, cFFR also has the advantages of not requiring preparation so is quickly obtained, and is easily applicable in the catheter laboratory regardless of the amount, choice, or method of contrast injection, as well as being absent of side effects, inexpensive and widely available.

The CONTRAST study [7] was a multicentre prospective cohort study that compared cFFR, resting Pd/Pa and iFR for predicting FFR and found that the diagnostic accuracy of cFFR was superior (86%, AUC: 0.93) than either iFR or Pd/Pa (80%, AUC: 0.88) for predicting ischaemic FFR. The optimal cFFR cut-off was 0.83 [7,8]. The Memento-FFR study [8] was a multicentre, retrospective pooled analysis that compared the accuracy of cFFR to Pd/Pa in predicting ischaemic FFR. The correlation between cFFR and FFR was stronger than between Pd/Pa and FFR (cFFR: $r = 0.9$, AUC: 0.95, Pd/Pa: $r = 0.79$, AUC: 0.90). On receiver operator curve analysis, the accuracy of cFFR was significantly higher than Pd/Pa for predicting FFR ($p < 0.001$).

Leone et al. [9] reviewed the evidence for cFFR, in comparison to resting Pd/Pa and iFR, as an alternative to conventional FFR for predicting functional lesion severity. They found that cFFR has the best correlation with conventional FFR than any resting index, and thus concluded that cFFR is a more accurate alternative for the assessment of flow-limiting CAD than the available resting indices. Furthermore, they concluded that compared to a hybrid approach using either cFFR, or Pd/Pa, or iFR to limit conventional FFR to doubtful cases, avoidance of adenosine is greatest with cFFR (67% of lesions (cFFR) vs. 55% (Pd/Pa), vs. 50% (iFR), in the CONTRAST study [7] and 78% (cFFR) vs. 56% (Pd/Pa) in the MEMENTO-FFR study [8]).

Leone et al. [9] have proposed an algorithm to implement a hybrid cFFR/conventional FFR strategy, which uses a cFFR cut-off of ≤0.83 for predicting a significantly ischaemic lesion, and a cut-off ≥0.89 for predicting a non-ischaemic lesion. In the proposed algorithm measurement of FFR with adenosine is limited to lesions with 'grey zone' cFFR (0.84–0.88).

cFFR has not yet been tested in a randomised controlled trial with clinical endpoints. This question becomes all the more relevant since a recent pooled analysis of the DEFINE-FLAIR and iFR-SWEDEHEART trials identified that iFR-guided management may not be non-inferior to FFR-guided management for death and MI [10]. The cFFR strategy lacks

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commercial support, as cFFR is independent of a dedicated software and may be perceived as being less novel and less commercially tractable.

FFR-guided management continues as the reference approach for functional lesion assessment in the catheter laboratory and of the available indices only FFR-guided PCI has long-term (5-year) data for reducing death, myocardial infarction, or urgent revascularisation compared to medical therapy alone. cFFR has superior diagnostic value over resting indices for flow-limiting coronary artery disease, as defined by FFR. Should a future clinical trial provide evidence of incremental value of cFFR-guided management for economic outcomes, and long-term health outcomes, over resting indices, then cFFR could be recommended in practice guidelines as a pragmatic, standard approach for invasive functional lesion assessment. Expanding the evidence-base in this way should enhance objective decision-making in invasively managed patients with coronary artery disease.

Disclosures

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