

The great iFR vs. FFR debate: why sometimes “the wait and see approach” is the best tactic as the best pragmatic solution will always emerge and become established

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With the publication of two “Letters to the Editor” in this issue relating to instantaneous wave-free ratio (iFR) papers, namely an ADVISE online publication and a hybrid iFR-fractional flow reserve (FFR) decision strategy, I would like to share with you my point of view¹⁻⁴.

In 1982, at the ACC, a furious debate took place between Andreas Gruentzig and John Simpson. John had just introduced the steerable, movable guidewire and in doing so eliminated the possibility of recording the distal pressure. During the debate, Andreas Gruentzig argued that it would be a major mistake to eliminate from the PTCA hardware the capability to record a gradient across the lesion. At that time, the presence of a gradient between the distal extremity of the balloon and the guiding catheter was the proof that one had crossed a significant lesion, and the disappearance of this gradient after the deflation of the balloon was the proof that one had performed an appropriate dilation.

The Gruentzig balloon had a two-centimetre fixed wire glued at the extremity of the balloon. In the catheter, a double channel existed: one to inflate the balloon and the other to record the pressure at the distal extremity. History has told us that the steerable, movable guidewire was the way forward and throughout the world the entire interventional community adopted the use of the steerable movable guidewire.

Then, about 10 years later, the RADI company (Sweden) provided an interventionalist cardiologist from Gothenburg, Håkan Emanuelsson, with a pressure wire. During his sabbatical, time spent in Rotterdam, we tested the device in 30 patients and found a significant but weak correlation between mean pressure gradient and percent area stenosis ($r=0.69$, $p<0.001$)⁵. The closest relationship, though, was found with stenotic flow reserve (SFR), which is an integrated parameter calculated from QCA, coincidentally created by Lance Gould. The relationship can be described by the equation: $\Delta P=65.2-12.6.SFR$ ($r=-0.79$; $p<0.001$), remember that it was a prehistoric period compared with respect to FFR now. With a measured gradient of >15 mmHg, the sensitivity was 94% and the specificity 96% to predict an SFR <3.5 . It was concluded that “the independent information obtained by pressure gradient measurement may be of particular value in intermediately severe lesions or in stenoses where the angiographic assessment otherwise is difficult.”⁵

In the same year, in May of 1993, combining the pressure wire and the velocity wire we published a new methodological approach for the assessment of coronary haemodynamics of both pre- and post-intervention⁶. Although we had duplicated in humans what had been demonstrated in the experimental animal model, we did not foresee the large application of this physiological tool in clinical practice. It was to

the credit of Nico Pijls and others to establish the experimental basis of determining maximum coronary, myocardial, and collateral blood flow by pressure measurements. Nico visited me at the Thoraxcenter and graciously asked me to be associated on this paper as co-author with van Son, Kirkeeide, De Bruyne and Gould⁷. I politely declined since the originality of his approach was unique, and was certainly strong enough without the need, at all, of my scientific endorsement. One year later, Carlo Di Mario and I described a new index, concluding that this new parameter could distinguish between arteries with and without coronary stenoses and had a significant inverse correlation with the severity of the stenosis⁸. Nevertheless, this index could not be used in daily clinical practice and was also not advocated as a pragmatic assessment of coronary stenosis.

In the meantime, Nico Pijls and Bernard De Bruyne gave solid foundation to the FFR by reporting in the NEJM the validation of the FFR when compared to noninvasive tests commonly used to detect myocardial ischaemia⁹. They established a firm cut-off criteria of 0.75 for the FFR parameters. One aspect of FFR that over time has been easily overlooked is this cut-off criterion of 0.75. Let's be honest, it's easy to remember, we know the history of CFR and the endless and never-ending search for an adequate cut-off point: 2.5 or 2.2 or 1.7. Nico and Bernard avoided this erratic search with a definitive, single and stable criterion. They became involved in a missionary crusade to convince the entire world of the incremental value of this technique for clinical practice. I told them it would take one to two decades to convince the world...and indeed, between 1993 and 2013, they succeeded in convincing the interventional community.

However, the seeds of contest were sown when papers were published from groups in London (Justin Davies) and Madrid (Javier Escaned) reassessing the coronary index^{10,11}. So we were not surprised to see Carlo Di Mario, Justin and Javier joining together with the publications of ADVISE and, most recently, CLARIFY^{2,4,12,13}.

And now, we come to the crux of the matter.

You as an interventionalist will have to choose one party based on your educated guess between conclusion A – instantaneous wave-free ratio and fractional flow reserve have equivalent agreement with classification of coronary stenosis severity by hyperaemic stenosis resistance¹³ – or conclusion B – diastolic resting myocardial resistance does not equal mean hyperaemic resistance, thereby contravening the most basic condition on which instantaneous wave-free ratio depends¹⁴, both ironically published in the same issue of JACC.

We understand the malaise of the pioneers seeing their established techniques being questioned, particularly painful when you consider the long path they have travelled with FFR, but also recognise the difficulties of the young generation of clinical scientists as the correspondence to the Editorial Office in this issue attests to^{1,3}.

For the time being, I have to give you one piece of advice. Don't succumb to emotion but rely on the pragmatic adoption of the interventional community who are going to judge by themselves, applying their clinical experience.

In the end, the future will tell us... so let's reconvene next year... and if not then, in 2023!

Ideas don't stop here

This journal is committed to you, our readers, and the open exchange of your ideas about our specialty. On the occasion of EuroPCR 2013, please join us on the EuroIntervention website and take part in the EuroIntervention survey! Please scan the QR code to have access to the online survey.



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