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Society of Cardiology guidelines recommend a FFR ≤0.8 to define a significant stenosis.

The pressure gradients in iFR measurements can be smaller, leading to a larger relative effect of absolute pressure changes caused by hydrostatic pressure. However, this phenomenon is frequently counterbalanced by a significantly lower systemic pressure during hyperemia in FFR measurements that magnifies the relative effect of absolute pressure changes. Consequently, the influence of hydrostatic pressure is not a matter of iFR or FFR—it affects both methods.

The transferability of intracoronary pressure measurements performed in a supine position to the clinical situation of an upright patient is a general limitation of all intracoronary measurement methods. What matters is that revascularization decisions are largely based on whether observed FFR or iFR values fall below or above the respective cutoff values. Operators should be aware of inaccuracies deriving from variations in hydrostatic pressure associated with anatomic stenosis location.

In conclusion, we must have the strength to critically appraise the tools we use in clinical practice. Such assessments are not criticisms of FFR or iFR, but a measure of how physics affects the measurements. The influence of hydrostatic pressure has clinical relevance in intermediate stenoses, and implementation of hydrostatic pressure into intracoronary measurement algorithms would further improve the methodological accuracy.

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Aspirin Versus Aspirin Plus Clopidogrel as Antithrombotic Treatment Following Transcatheter Aortic Valve Replacement With a Balloon-Expandable Valve

With the ARTE (Aspirin Versus Aspirin + Clopidogrel Following Transcatheter Aortic Valve Implantation) trial Rodés-Cabau et al. (1) added eagerly awaited evidence regarding the optimal antithrombotic regimen in patients after transcatheter aortic valve replacement (TAVR). The investigators revealed that single antiplatelet therapy with aspirin reduces the risk of bleeding as compared with dual antiplatelet therapy with aspirin and clopidogrel. Incidence of ischemic events such as acute myocardial infraction or stroke did not differ between groups.

It is well known that there is substantial interindividual variability in pharmacodynamic response, especially to clopidogrel medication. Impaired pharmacodynamic response to antiplatelet medication is called high on-treatment platelet reactivity (HTPR). Several factors have been reported to be associated with HTPR, including diabetes mellitus, increased age, drug-drug interactions, and high body mass index. Therefore, in a recent study we hypothesized that the incidence of HTPR is high in TAVR patients as they are old, multimorbid, and polymedicated. Indeed, we were able to reveal that HTPR to clopidogrel occurs in nearly two-thirds of TAVR patients (2). Taken together with the results of the ARTE trial, one could hypothesize that even residual clopidogrel antiplatelet effects may increase the risk of bleeding, without reducing ischemic events.

In TAVR patients, ischemic events are rare and bleeding events are more frequent. However, Hansson et al. (3) recently reported the incidence of transcatheter heart valve (THV) thrombosis to be

7%. THV thrombosis often remains subclinical. However, Ghanem et al. (4) reported that subacute subclinical brain infarctions after TAVR occur in 61% of patients and are associated with impaired long-term cognitive function. Unfortunately, THV thrombosis was not assessed in the ARTE trial. Chakravarty et al. (5) recently reported in an observational analysis that oral anticoagulation is superior as compared with antiplatelet medication in reducing the incidence of THV thrombosis. Currently, randomized controlled trials such as GALILEO (Global Study Comparing a rivAroxaban-based Antithrombotic Strategy to an antipLatelet-based Strategy After Transcatheter aortIc vaLve to Optimize Clinical Outcomes) (NCT02556203) and ATLANTIS (Anti-Thrombotic Strategy After Trans-Aortic Valve Implantation for Aortic Stenosis) (NCT02664649) investigate a dual antiplatelet therapy versus an anticoagulation-based regimen in TAVR patients.

Based on currently available data, additional clopidogrel treatment after TAVR seems highly questionable. Still, further trials investigating the optimal antithrombotic regime after TAVR are needed.

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REPLY: Aspirin Versus Aspirin Plus Clopidogrel as Antithrombotic Treatment Following Transcatheter Aortic Valve Replacement With a Balloon-Expandable Valve

We have read with interest the letter from Dr. Piayda and colleagues on the recently published ARTE trial (1). We agree with the authors on the importance of adding evidence-based data to the complex field of antithrombotic therapy following transcatheter aortic valve replacement (TAVR). We think that the results of the ARTE trial showing both the lack of benefit for ischemic events and the harmful effects for bleeding complications of dual (vs. single) antiplatelet therapy represent an important step forward in the field (1).

Dr. Piayda and colleagues referred to the variability of platelet reactivity to clopidogrel among TAVR candidates, with up to two-thirds of the patients exhibiting high on-treatment platelet reactivity. However, other authors failed to replicate such results and reported a much lower (~40%) incidence of high on-treatment platelet reactivity among TAVR patients (2). Also, Watanabe et al. (3) showed that about one-third of patients undergoing TAVR presented a hyperresponse to clopidogrel therapy leading to very low platelet reactivity, and this was associated with an increased rate of severe bleeding events. This reflects the high variability of platelet reactivity according to different TAVR populations and tests used for its measurement, and diminishes the potential value of these tests in the context of TAVR. In fact, the principle of individualized antiplatelet treatment based on platelet reactivity tests has already failed in the coronary field (4), and the possibility of implementing such tests in the TAVR arena and obtaining clinically meaningful results is extremely slim.

Another aspect pointed out by Dr. Piayda and colleagues relates to subclinical valve thrombosis post-TAVR. The occurrence of subclinical valve