In their recent editorial, Rao and Nolan (1) decided to ignore the well-known relationship among experience, volume, and medical outcomes and played the dangerous game of rejecting an important hazard signal that, if tackled properly, could better the outcomes of patients undergoing heart catheterization. Our data demonstrated an increase in the rate of femoral vascular access-site complications (VASCs) after the widespread adoption of radial access (RA) that persisted after multivariate adjustment. This increase in femoral access (FA)-related VASCs was numerically so relevant that it offset the benefit of RA at the overall population level. We concluded that approximately one-half of VASCs occurring in patients undergoing FA are attributable to the adoption of RA (2). However, Rao and Nolan went so far as to ascribe a causality dimension to attributable fractions (“by using the term attributable, the authors imply causation—that the radial approach caused femoral complications” (1)). Their statistical faux pas translates a defective understanding of the concept of population attributable fraction (PAF), which is defined as the proportional reduction in average disease risk over a specified time interval that would be achieved by eliminating the exposure(s) of interest from the population, but does not address the probability of causation for a specific disease or event (3). A clear and extensive dissertation on the concept, use, and misuse of PAF is provided by Rockhill et al. (3). The widespread adoption of RA in the clinical arena has coincided with other important changes (such as the increase in procedural complexity and patient risk profile) that have all contributed to increase the risk for femoral VASCs in patients undergoing cardiac catheterization. Our observation that the VASC rate in patients undergoing FA has increased, in comparison with the “pre-radial era,” had also been hinted at by an analysis of a large (1.4 million patients) cohort of the National Cardiovascular Data Registry: the risk for FA site bleeding increased as a function of the relative increase in RA adoption over a 3-year period: from 6.3% in the very low adoption group (<2% of RA percutaneous coronary interventions) to 7.4% in the high-adoption group (~45% of RA procedures). Although stating that a causative relationship exists between the introduction of RA and the VASC rate increase in FA patients is not supported by the available evidence, these findings nevertheless warrant reconsideration of the indications of FA and improvement of FA technique in the contemporary practice.

The overwhelming benefits of RA are not to be discussed. The radial artery is and must remain the default approach in most patients undergoing cardiac catheterization. The question now becomes how to achieve safer FA when it is needed. As appropriately pointed out by Dr. Harbaoui and colleagues, reducing the number of FA procedures will translate into a lower overall VASC rate because of the lower risk associated with the use of RA. However, we are uncertain if the linear relationship proposed by Harbaoui and colleagues can reliably estimate of the exact figures of VASC rates in a real-world population, as one could expect an exponential increase of the VASC rate in FA patients as FA volume goes down. Additionally, our contemporary cohort is meant to represent the transition from FA to RA that, at our institution, took place almost a decade ago. Nowadays, patient clinical profile and procedural factors might be markedly different. Therefore, a scientifically sound estimation of the actual contemporary VASC rates with FA and RA might be provided only by replicating our study with data from a current cohort.

In the current radial era, we think that the focus of the scientific community should be on the improvement of FA techniques among trainees and the maintenance of adequate FA volume among established interventional cardiologists, while, as appropriately recommended by Dr. Harbaoui and colleagues, striving for the extension of RA indications. In this ideal scenario, the safer RA would be used in the overwhelming majority of cases, and the potentially more dangerous FA would be performed by skilled operators in a very small proportion of patients.

There are several important lessons to be learned from this ongoing discussion. First is that causation cannot be assumed from observational data, not even when used in the context of an attributable fraction. Second is the importance of backing up opinions with objective data, not expertise alone. Third, and perhaps most important, is to diligently consider safety signals and explore how these signals can be addressed to improve the quality of care.

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DCB and Dissections
In Search of a Good Balance Between Enthusiasm and Scientific Strictness

Byrne and Joner (1) recently wrote an elegant editorial comment on a study that our group recently published in *JACC: Cardiovascular Interventions* (2). We have to thank the 2 experts for their kind words regarding the importance of this type of proof of concept, independent study. However, while reading the editorial, we made several observations that may be of some help for future discussions, which we summarize in the following points:

First, despite their enthusiasm for stents, Byrne and Joner (1) should have also mentioned one of the major drawbacks of this technology, namely, the risk of very late (and never-ending) stent thrombosis. This concern has been shown to be a serious issue indeed, of very late (and never-ending) stent thrombosis. This major drawback of this technology, namely, the risk of vessel closure after delivery of paclitaxel, given at a single-burst dose on the vessel wall, might facilitate vessel healing (3). Further studies will hopefully clarify this intriguing hypothesis.

Second, we “enthusiastic adopters” of drug-coated balloons would like to underline that this technology in not “against” stents: on the contrary, it should be considered an adjunctive and complementary tool that should be available on the shelves of our catheterization labs: for example, but not exclusively, when you feel a stent is not the best choice, namely, if the vessel is too small, when avoiding jailng a major side-branch appears reasonable, or if you already have several stent layers there as a result of recurrent in-stent restenosis.

Third, we concur that the results of our study should be considered as hypothesis-generating. However, some pre-clinical data also seem to confirm that paclitaxel, given at a single-burst dose on the vessel wall, might facilitate vessel healing (3). Further studies will hopefully clarify this intriguing hypothesis.

Fourth, we fully agree with Byrne and Joner (1) that current guidelines still do not suggest drug-coated balloon use for native coronary vessels, but Byrne and Joner (1) should also mention that several expert consensus papers give clear indications for their use in this setting (4,5). We can only speculate on why the international guidelines do not reserve drug-coated balloons a role in native vessels yet.

Results of several currently ongoing clinical trials are eagerly awaited to definitively answer this important question.

In conclusion, we are well aware of the limitations of our study and we concur that stronger scientific evidence is required before a change in clinical practice may be recommended. However, we strongly believe that small, independent, well-designed pilot studies are necessary to advance the field and draw the line for additional larger studies able to provide definitive clinical evidence.