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Stable angina: to stent or not to stent?

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"To be, or not to be, that is the question."
The Tragedy of Hamlet, Prince of Denmark – Act 3, Scene 1
William Shakespeare

At the dawn of the 17th century, Shakespeare wrote what would become one of the most well-known lines of his plays: uttered by Prince Hamlet, who was contemplating death and suicide, "to be, or not to be" might essentially be interpreted as "to act, or not to act." On one hand, Hamlet was certain about the pain, sorrow, and unfairness of life; on the other hand, however, there was the uncertainty of death being able to end all of his sufferings. *That was the question…*

Almost 400 years later, the German radiologist Andreas Grüntzig (1939-1985) *acted* and performed the first coronary angioplasty in a conscious patient, and, from that day on, a new field was born, and interventional cardiology has since reshaped modern cardiovascular medicine. Percutaneous coronary intervention (or PCI) has become one of the commonest procedures in medicine and, in patients with acute coronary syndromes, it significantly impacts outcomes if performed in a timely fashion. Still, the clinical benefit of PCI in patients with stable angina has been continuously revised as medical therapy continues to evolve. In this issue of *Heart & Metabolism*, a critical, unbiased appraisal of the role of PCI in patients with stable angina will be presented to our readers.

We start our journey by reading the article by Prof Boden about the messages two audacious clinical trials—ORBITA and ISCHEMIA—may have to share. For many years, cardiologists have accepted the concept that if there is angina and/or myocardial ischemia, there must be coronary stenosis. Therefore, treatment should be aimed at finding the lesion and fixing the artery by PCI if feasible. The already published and much discussed ORBITA trial adds to a list of previous clinical trials (COURAGE and BARI-2D, for instance) in which the benefit of PCI in patients with stable angina was very limited if present at all. The ISCHEMIA trial is eagerly awaited, to further enrich our knowledge about the prognostic impact of revascularization in stable patients with moderate-to-severe myocardial ischemia.

Another contribution from the cath lab is the determination of FFR (or fractional flow reserve) which, in theory, by providing a more physiological assessment of coronary stenosis, could be used to guide myocardial revascularization. Prof Perera discusses this topic in his article and tells us about the principles and pitfalls of FFR, and how clinical trials based on FFR may have overestimated the benefits of FFR-guided revascularization in terms of hard end points.

As PCI became more widely used in patients with stable angina, the unexpectedly high rates of early recurrence or persistence of angina after PCI served as a reminder that stable angina is not a single disease, but rather a complex multifactorial pathophysiological

process. Prof Marzilli and I present our thoughts on the subject, highlighting that, besides the high incidence, many PCIs in patients with stable angina are deemed inappropriate according to current guidelines and accompanied by an intrinsic risk of complications. Moreover, patients with post-PCI angina are at higher risk of cardiovascular events and represent an economic burden on the health care system.

If PCI ought to be offered to patients unresponsive to optimal medical therapy, Prof Marzilli returns to explain that any optimal medical strategy should follow a couple of principles, including a match between the main pathophysiological process related to myocardial ischemia and the mode of action of the selected antianginal drug; safety, tolerability, and lack of drug interactions should be considered; and the clinical profile/comorbidities of the patient acknowledged. He is urging us to have a more individualized approach to treating the patient with stable angina as opposed to the "one size fits all" approach.

Next, we learn from Prof França Neto that, if PCI is clearly indicated in a patient with stable angina, the cardiac cell should not be forgotten as a therapeutic target for protection using trimetazidine. This unique agent will, by shifting the production of ATP from the free-fatty acid oxidation pathway to the more efficient glucose oxidation pathway, reduce oxidative stress and membrane damage, reduce myocardial injury, reduce the occurrence/severity of post-PCI angina, and might favorably impact major adverse cardiac and cerebrovascular events in post-PCI patients.

Another task I was given in this issue was to share a clinical case of a patient with stable angina in which a decision had to be made between placing a stent or keeping the patient on optimal medical therapy as the most effective strategy for symptom control.

In the Refresher Corner, we invited Prof Berwanger to explain what the criteria are for composite end points in clinical trials and why they matter. As we follow more and more clinical trials being presented during medical meetings and/or published in highly respected journals, it is important that we try to fully understand the chosen end points because they will directly influence the interpretation of the main results of the trial and, as such, the potential clinical application of the new data being generated.

Finally, Prof Soufiani was invited to shed some light on the everlasting debate on choosing between functional and anatomical imaging in the assessment of a patient with stable angina, particularly at the initial evaluation.

I believe that the opening phrase of Hamlet's soliloquy should invite us to pause for reflection before referring a patient with stable angina for PCI. If there's no clear benefit in preventing death and/or myocardial infarction, and symptom-relief may be short-lived in patients with stable angina, I'd dare to say that more often than not we would choose *"not to act."* But, in doing so, we must *"act"* to offer our patients the most effective combination of antianginal drugs and disease-modifying agents, tailored to the needs of each and every patient.

If I could have a word with Hamlet, I believe I know what I´d have to say to him… ■