**Title: CRT 23: The FAST III Randomized Controlled Trial**

**Participants: Dr Joost Daemen**

**Date: 17th March 2023**

**Dr Joost Daemen**

"- My name is Joost Daemen, I'm an interventional cardiologist in the Erasmus University Medical Centre in Rotterdam, the Netherlands.

**Study Rationale**

So numerous studies have established the role of physiology-guided PCI in patients with intermediate coronary artery lesions in the absence of positive noninvasive ischemia testing. And that actually has resulted in a level of evidence caused one recommendation to perform either FFR or instantaneous wave-free physiological lesion assessment in the absence of a positive non-invasive ischemia test. That said, physiology is still underutilised in clinical practice with an average number of around 20% in clinical cases which is likely not the percentage that it should be based on these guidelines. This low number has been hypothesised to be due to longer procedure times, cost needed to use these devices, the invasive nature of the pressure wire, the use of hyperemic agents with known side effects to the patients. And that actually was a little bit the background of of finding simplified means to do physiological lesion assessment. And that's where angiography based physiology is coming into play, which is a technology that uses two orthogonal angiographic projections and simplified computational fluid dynamics that are being applied to a 3D reconstruction of the coronary artery of interest to calculate a pressure grading across a specific segment in a coronary artery of interest. So in the past decade, several of these indices have been validated and one of them is vFFR, which is vessel FFR which is the index of gas workstation software developed by biomedical in Maastricht. So vFFR proved to be very accurate alternative to pressure wire based FFR measured in an invasive setting. Several validation studies have been performed as of today, so far one was the initial single centre with respect to validation in 100 patients. That was subsequently extended to a multi-center project in five sites across the globe in which we validated the use of vFFR in a cohort of 330 patients. And we were again able to confirm that offline computated vFFR with the help of a blinded core lab correlated very well to invasive pressure wire based FFR with sensitivity and specificity figures of around 90% when computated on site, so by the individual sites. That of course, in the theory should in the future should be able to do these computations. We found more or less identical figures with an area around the curve above 85 and also sensitivity and specificity figures very well in the range of where you would like them to be as an alternative to FFR. Thus far, however, outcome data is lacking and that's where the FAST III study is coming into play.

**Patient Population and Study Design**

So FAST III is a multi-center international outcome trial designed to study whether a vFFR guided revascularization strategy is non-inferior to a pressure wire-based FFR guided revascularization strategy in patients presenting with either stable angina, unstable angina, NSTEMI, or stabilised setting for a non-culprit lesion after a STEMI. The study is being conducted in seven countries, 35 sites, and designed with the primary endpoint of MACE, being all-cause death. Any repeat myocardial infarction and any repeat vascularization at one year post randomization. At present, we started enrolling end of November, 2021. We started activating sites at present are 28 sites active in seven countries and by now we have enrolled almost 650 patients within the sites. We're still activating more sites and hope to end enrollment by the end of 2023.

**Potential Impact of the Results**

So non-inferiority of vFFR as compared to FFR would establish the role of angiography-guided physiology and vFFR in particular in guiding revascularizations in patients with intermediate coronary artery lesions presented to the cath lab in the absence of positive non-invasive ischemia testing. That could have a tremendous implications in terms of patient management. There are a lot of secondary endpoints in the trial focusing on safety of both procedures, feasibility, but also cost effectiveness because as you can imagine the the application of angiography-based physiology would preclude the need for PCI equipment. So no guiding catheters needed, no invasive manoeuvring With a pressure wire, you can still stay lower with your heparin. So all and then there is no need for a hyperemic agent which could enhance the speed in which standard physiology guided angiography is performed and could have implications for cost effectiveness and could also have, but that we don't know implications in terms of patient safety. So we know that these guiding catheter equipment pressure wires carry a low but not negligible risk of of adverse events simply caused by the invasive manoeuvring by a pressure wire. So that is something that we will learn from FAST III as well as several other trials on the topic that are ongoing today. Next, to these potential impacts on cost effectiveness and safety, the demonstration of the feasibility of a vFFR guided revascularization strategy could have important implications for catheterization laboratories across the globe that do diagnostics only. For instance, in our region we have a lot of sites that do that. That would mean they could, by doing proper angiography doing a physiological lesion assessment without the need for PCI equipment and streamline thereby their patient management heart team referrals as well as decrease the time delay that could be introduced by these interdisciplinary discussions among sites. And finally, a non-inferiority of the trial could also enhance future research in terms of heart team decision making in general in patients in which there is an angiography but no invasive physiology assessment of intermediate artery lesions.

**Next Steps**

So as mentioned FAST III is currently enrolling in 27 sites. We're still activating sites and we hope to finish enrollment by the end of 2023. With the one year endpoint, we hope to be able to present the results end 2024 or likely early 2025. And with that in mind, we hope that there is a potential chance of having significant impact on future revascularization guidelines.”