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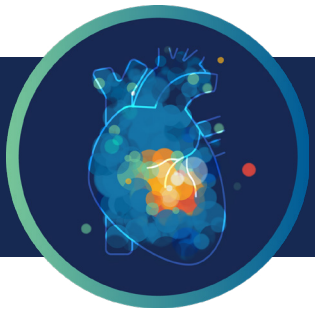
# EXPERT INSIGHTS: Q&A WITH DR. AMIR KAKI



**Dr. Amir Kaki, MD, FACC, FSCAI**

*Associate Professor Wayne State SOM*

*Director, Mechanical Circulatory Support*

*Director, High-Risk Complex Coronary Interventions*

*Associate Director, Interventional Cardiology Section Ascension St John Hospital, Detroit, USA*

Access the full publication:
**Microaxial Flow Pump or Standard Care in Infarct-Related Cardiogenic Shock**

## What are your key take aways from this trial and has it changed your clinical practice when managing patients presenting with ST-elevation myocardial infarction (STEMI) complicated by cardiogenic shock?

Many of my colleagues and I have been working to advance best practices for the use of Impella (Abiomed, Johnson & Johnson MedTech, Danvers, MA) in both high-risk percutaneous coronary intervention (PCI) and acute myocardial infarction (AMI) cardiogenic shock, including colleagues working with the National Cardiogenic Shock Initiative (NCSI). We have all been involved in prospective data collection, that have refined our best practices and advanced our understanding of strategies to improve mortality in cardiogenic shock secondary to AMI.

The data from DanGer has been wonderfully validating. Those of us who have long believed that circulatory support is a key part of managing patients with shock are vindicated since we have endured much criticism from others because of the absence of robust data from a randomized controlled trial. But the journey doesn't end here. Continuing to improve the care of patients with a focus on the reduction of adverse events is a significant focus for us as educators and operators as we move forward. Our commitment to this cause remains unwavering, and we are motivated by the potential to make a real difference in patient outcomes.

## Would you change the per protocol definition of cardiogenic shock used for enrollment to the DanGer Shock trial?

Optimizing the design of the first trial to demonstrate a mortality benefit with mechanical circulatory support (MCS) was critical. Dr. Jacob Moeller and his colleagues are to be commended on identifying a very sensible population to study and meaningful for the clinical community. A focus on STEMI-related shock, which is primarily related to left ventricular dysfunction, in the absence of coma from cardiac arrest, was an excellent selection for the first MCS trial. Future investigations might investigate other populations of non-STEMI or non-acute coronary syndrome related shock, but I would certainly keep everything the same with respect to the existing inclusion criteria for the DanGer trial.

## The authors and all involved in this study should be congratulated for the resilience and determination shown in getting this trial to the finish line a decade after the first patient was enrolled. What are your thoughts on the open-label design and the ability to randomize patients before revascularization, after revascularization (but in the catheterization laboratory) or ≤12 hours after having left the catheterization laboratory? Are we comparing apples with apples by randomizing patients at different time points during the treatment of a STEMI?

Embedded in the question are several individual questions, I will try to answer them individually. How

would it be possible to evaluate a patient in shock with any device in a blinded manner? These patients are critically ill and on the verge of death; conducting a trial, such as a sham control trial, would be impossible in the setting of shock. The rigorous attention to inclusion and exclusion criteria and the formal randomization strategy is adequate to completely answer the primary question that was addressed by the hypothesis.

Does routine use of an Impella CP in STEMI-related shock reduce mortality at six months? The question about timing fails to recognize the reality of patient treatment in STEMI. The investigators are randomizing all patients at the time of shock diagnosis (when shock inclusion criteria are met), which could happen at different time points during the treatment of STEMI. All patients coming in with STEMI that will develop shock, do not necessarily have shock at the time of their initial hospitalization or entry into the cardiac catheterization laboratory. Studying patients that develop shock during presentation or early in their initial course of STEMI is a very reasonable and useful way of advancing our knowledge about outcomes in shock. The effect of randomization allows us to adequately compare these groups.

**Why do you think the composite safety endpoint was significantly higher in the microaxial flow pump group versus the standard of care group? Can it all be blamed on the steep learning curve associated with using this device effectively?**

The adverse events were certainly higher than we'd like to see in any of our patients. However, there are two critical points worthy of consideration. Despite the adverse events, there was a survival benefit.

Secondly, it's important to note that the rates were similar to rates of prior shock studies with the intra-aortic balloon pump (IABP) and extracorporeal membrane oxygenation (ECMO), and importantly, those studies only evaluated patients for one month. The DanGer study evaluated patients for six months, so the interval for evaluation was six times longer, capturing more adverse events. Continued efforts to improve bleeding and vascular complication rates are important and part of our mission in educating our colleagues on best practices, which we expect will dramatically lower adverse events rates.

Additionally, in our practice, we value the clinical support from the Abiomed clinical support team. In the US, enlisting their support both in the cath lab and at the ICU bedside is common. Clinical support staff and remote monitoring and the use of the 24-hour clinical support center are all important resources to provide patients on MCS with the best chance of recovery. European physicians generally do not use these resources, which may have contributed to some of the adverse event rate differences and higher reported events than we commonly see in the US.

**Ultimately this was a small trial that recruited patients from Denmark, Germany and the United Kingdom. Can the trial outcomes, therefore, be generalized for instance to the United States and/or the America's as a whole?**

This was the first ever to successfully demonstrate a mortality benefit with statistical significance, and a number needed to treat of eight. Referring to it as a small trial is not really accurate since it was adequately powered for statistical significance and achieved that goal as well as answered the hypothesis regarding mortality. The outcomes of this trial, therefore, hold great significance and should be of interest to all of us. Additional data is certainly always welcome, but the planned RECOVER IV study that would have randomized patients in the United States, which had already begun prior to the completion and reporting of DanGer has now been stopped due to the decision by the safety and monitoring board of that trial which concluded that there is no longer equipoise to randomize patients with AMI cardiogenic shock to a non-Impella treatment arm. As a result of DanGer, I suspect the guideline writers will advance the recommendation of Impella use in AMI-related cardiogenic shock.