On the Frontline of TAVR Research: An Interview With Michael Reardon, M.D.

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Michael J. Reardon, M.D., is a cardiac surgeon at Houston Methodist Hospital. He began performing surgical aortic replacements in the 1980s and did his first transcatheter aortic replacement (TAVR) in 2011 in the CoreValve trial for high-surgical-risk patients. Since then, Reardon has been at the forefront of TAVR research, serving as principle and co-investigator on multiple TAVR clinical trials. He is currently the surgical national principal investigator for the Medtronic CoreValve SURTAVI trial investigating all-cause mortality or disabling stroke in TAVR vs surgery for intermediate-risk patients and the Medtronic EVOLUT trial for low-risk patients. Reardon is also the national principle investigator for the Boston Scientific Reprise III trial for the Lotus TAVR Valve.

Reardon recently coauthored a review of TAVR outcomes in the *Methodist DeBakey Cardiovascular Journal* with Dr. Manuel Reyes. I sat down with each author in August to ask them about their experiences with TAVR and advice for fellow physicians interested in the technology. This transcript has been edited for clarity and length.

What was your initial reaction when you started performing TAVR?

MR: When I first heard about TAVR when the earliest research was being done in labs in the late 1990s and early 2000s, I thought it was crazy. I thought, "There is no way this will ever work." Now, the good news is that I've been wrong so many times in my life that I've learned to keep an open mind. When we did our first couple TAVRs, I was shocked at how quickly we saw improvement. Because patients didn't undergo the trauma of surgery, the relief of aortic stenosis was instantaneous. We could watch the heart on echocardiogram instantaneously get better. Remember, we started this with people who were so sick that they were either not surgical candidates or were high-risk surgical candidates. Yet we would do these TAVRs and two days later the patients looked normal. It was really quite shocking and gratifying at the same time.

Was there a particular patient or outcome that stands out as a turning point in how you viewed the prospects of TAVR for aortic stenosis?

Michael J. Reardon, M.D.

MR No, it was really pretty clear early on that this was going to work. This is how I explain it: Aortic stenosis is when your aortic valve narrows down. As this valve gets smaller, it's like going in the backyard and putting your thumb over a hose. The more you cover it up, the more pressure builds up behind your thumb—that's what's happening in your heart. Now, imagine that you're spraying your hose at your kids with your thumb over it, and you take your thumb off. What happens? Instantaneously, the pressure goes down.

Now, if you did that, but I had to beat you with a stick at the same time, you may take a while to notice the relief. That's surgery. On the other hand, if you're just going to take your thumb off with me just tickling you, well that's TAVR. There's much less physiologic insult with TAVR.

And so, with surgery, your heart gets better right away, but it takes a while for your body to realize it's better. With TAVR, your heart gets better right away, and your body knows it's better right away.

How have the clinical trials for TAVR evolved over the last 10 years?

MR: The data from the TAVR trials in the United States is by far the best data we have ever gathered on structural heart disease. We started with the Partner B trial randomizing people who were not surgical candidates to compare TAVR to medical therapy, and TAVR did better. We saw a 20% improvement in survival and much improved quality of life. By the time we started CoreValve Extreme Risk, medical treatment had done so poorly that it was no longer ethical to randomize, so we tested an objective performance. We still beat that. Then, we moved to high risk for both the Partner A and CoreValve randomizing TAVR against surgery. Partner A was first, and the survival for surgery versus a catheter procedure was exactly the same for five years. Then we did CoreValve High Risk, and lo and behold, TAVR had a statistically superior survival to surgery. That was the first time we had ever seen statistically better survival for any interventional procedure over surgery. It was really quite a shock. We're out to three years now, and the survival is still better.

Next, we started testing TAVR on intermediate-risk surgical risk patients who had a risk of fatality with surgery of 3% to 10%. I ran the SURTAVI trial for Medtronic; my friends ran Partner 2A. In both trials, TAVR had a numerically better survival than surgery, but not statistically superior. But, you know, if you're looking at a less invasive procedure, you don't have to be better—you have to be just as good as. The tie goes to the runner, and TAVR wins.

Now we're doing the low-risk trials for people with a risk of 3% or less. There are currently two of these trials: the Partner 3 trial for the Edwards valve and Medtronic EVOLUT Low Risk, which I run with Jeff Popma.

What was the reaction when TAVR beat surgery for survival in the CoreValve High Risk trial?

MR: When we found that TAVR was superior in the high-risk trial, everybody was stunned. It was the first time it had ever been seen. This was a big deal that a catheter-based procedure beat surgery for survival. Generally, catheter-based surgery procedures don't do as well as surgery for survival. If a catheter-based procedure can get close enough results to surgery, everyone accepts them because they're less invasive. This one was actually better.

How are the real-world trends for TAVR versus surgery changing?

MR: We now have FDA approval for nonoperative, high-risk, and intermediate-risk candidates. The interesting thing is that in the last quarter of 2016 there were more TAVRs than isolated aortic valve surgeries done in the United States, and that's before we had full approval for two valves for intermediate-risk patients. Those lines are going to deep diverging, and going forward we'll be doing more TAVRs than surgeries.

If these low-risk trials show non-inferiority and the FDA approves TAVR for low-risk patients, then by the time I retire, we will probably be doing three times as many TAVRs as surgeries.

How has TAVR changed the aortic valve replacement experience for patients?

MR: Thanks to TAVR, we've eliminated the ICU, and we do this under local anesthesia. My last TAVR patient today was awake and talking to us throughout the procedure, then she went to the recovery room for about an hour. She'll go to her room, and by dinnertime, she'll be walking around on the floor with her family like she's normal. Tomorrow, she'll look like we haven't touched her, and there's no way, no matter how small my incision is in surgery, that my patient would ever look that way.

How does learning TAVR compare to learning surgery?

MR: Surgery is a technical thing. To be an expert in a technical skill you need 10,000 hours of practice; you have to do it over and over and over again. On the other hand, TAVR is a technology. Technology is a lot easier to learn and become an expert in the technique. That means it will be easier to expand this technology to more physicians, like my interventional cardiology colleagues. Ultimately, that expands patient access. Right now, you may have to travel a long way to find an experienced surgeon. But since more doctors can learn TAVR than surgery, it may be easier for patients to find a TAVR doctor. I think it will be overall very good for patients.

What are some common patient concerns about TAVR?

MR: The biggest patient concern about TAVR is stroke. When we did the first trial that randomized against surgery in the U.S., which is the Partner 1A, stroke was actually twice as common with TAVR than with surgery—5% versus 2.5%. That was a huge conundrum because the survival was so good, but you had a risk of stroke. However, in the Medtronic High Risk trial, there was less stroke in TAVR than there was in surgery, and that trend has continued in every randomized trial since. We now know that stroke is no more common with TAVR than with surgery, and now we are even working on embolic protection devices such as filters to try and prevent even more strokes.

How does the durability of TAVR valves compare to surgical valves?

MR We don't know that yet. We have good data for five-year studies that show that TAVR valve durability is just as good as surgery, but five years isn't enough time. We really need 10 years. Looking forward, we'll follow patients for 10 years in both the intermediate- and low-risk trials that are now ongoing. So, hopefully, we're going to find out.

Who in healthcare do you most want to reach with information about TAVR, and what's the most important thing for them to know?

MR: I'd really like to reach both patients and primary care doctors. We know that if you have severe aortic stenosis and symptoms, if we don't do something, you're going to die. You're going to die at a rate of one to two percent per month. It's worse than most cancers! So, if you have severe symptomatic aortic stenosis, you fall under guidelines 1A, meaning we've got great evidence that you should have this fixed. And yet, when we looked at the numbers, 30 to 60 percent of people that had symptomatic aortic stenosis never got any therapy. Why? Because a lot of people thought, well, these patients are too old, we can't do the surgery. Patients often never made it to a surgeon or even a cardiologist to talk about their options.

Now, with TAVR, we're seeing more people coming in because now they know they have a less invasive option. In the last quarter of last year, we did more TAVRs than isolated aortic valves. The number of aortic valve surgeries hasn't fallen over the last five years; the TAVRs have just gone up. That means we're getting people coming out of the woodwork who, in the past, were just either not being offered treatment or avoiding treatment.

I want patients and doctors to know that in an institution like this, we can offer TAVR or the possibility of TAVR for anybody who is a candidate for a tissue valve. Now, if you're low-risk, I can't just throw a TAVR in you, but I have a trial where we randomize half to surgery and half to TAVR. Surgery's still the gold standard in low-risk patients, and you can come to a place like this where we have excellent results. But, at least you know you have the opportunity to potentially get TAVR. You'll get the latest and the greatest treatment.

I'd really like to reach out to the family practice docs out there that and tell them that if they have a patient who is 80 years old and are afraid to send them to surgery, that patient may not need surgery. They may be a good candidate for TAVR. If that's the case, we'll have them back to you in three days looking as good as new.

What should primary care doctors look for in patients as a sign that they should get a TAVR evaluation?

MR Anyone who meets the criteria for severe aortic stenosis on echocardiography ought to have a consultation with either a heart surgeon or a cardiologist. Ideally, they should come to a valve team. Here at our valve clinic, I don't see these patients in isolation, nor do my cardiologists. We see them together and discuss them as a multidisciplinary team. That way, we can offer patients a much broader toolkit and give them a well-thought-out team opinion on which tool is right for the individual patient.

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Conflict of Interest Disclosure
Laura Gerik is Assistant Managing Editor of the *Methodist DeBakey Cardiovascular Journal*