



Ganesh Manoharan

## Options for transcatheter aortic valve implantation: comparing self-expanding with balloon-expandable valves

The advent of transcatheter aortic valve implantation (TAVI) has offered clinicians the option of managing patients with severe symptomatic aortic stenosis, who are at high operative risk, the possibility of replacing the aortic valve without requiring a full open-heart surgery. Two technologies have been developed for the deployment of valves *in situ*: self-expanding and balloon-expandable valves. We spoke to Dr Ganesh Manoharan, Consultant Cardiologist at the Royal Victoria Hospital, Belfast, about these two types of devices to find out more.

Can you give us an overview of the differences between self-expanding and balloon-expandable valves?

**Dr Ganesh Manoharan (GM):** At present, there is only one commercially available balloon-expandable valve available, the latest iteration of which is the Edwards Sapien® 3 device (Edwards Lifesciences Corp., California, USA). In general, this technology involves a valve crimped or mounted on a balloon and, upon inflation of the balloon, the valve expands and assumes the position in the shape of a valve.

With the self-expanding version of valves, different technologies are available commercially but they generally comprise of a nitinol self-expanding frame supporting either a bovine- or a porcine-based pericardial valve. However, amongst the self-expanding valves, there is still a differentiator: the Medtronic CoreValve® (Medtronic, Inc., Minneapolis, USA) series is the only one that is supra-annular in function; all the other self-expanding valves are annular in function. The supra-annular valve position has important haemodynamic advantages.

The balloon-expandable technology, due to design characteristics, allows the clinician only one attempt at deploying the valve. You do not have the ability to reposition after valve deployment. You can reposition the valve prior to deployment to achieve optimal positioning, but once the balloon is expanded and valve deployment is complete, it is impossible to reposition, but

hopefully, it is in a good position. Rapid ventricular pacing and significant drop in blood pressure is also required during valve deployment.

Furthermore, once the valve and balloon exits the delivery sheath, the device cannot be retrieved again from the patient, so the clinicians are committed to deploying the valve.

The key advantage of self-expanding technology is the potential to either fully reposition or at least retrieve and, in the case of a recapturable system, resheath the valve up through about 90% of full release. This means that while the valve is still attached to the delivery system, the clinician can recapture and reposition it if they do not like where it is and, if they don't like the way it behaves, it can be safely removed from the patient. You can always argue, of course, that if you are careful and safe you don't need to retrieve the valve, but we work in an environment in which we are dealing with high-risk patients with challenging anatomies, and with multiple operative skills – having even one chance of being able to fully retrieve a device is a chance that adds to the overall safety profile and the benefit of the device, and ultimately for the patient. There is also no need for rapid ventricular pacing during deployment, thus reducing the risk of haemodynamic compromise.

How do you choose which valve to use in specific patients?

**GM:** At the moment we have both technologies on our shelf in our department. We use both

frequently enough to have gained the expertise in using both technologies safely.

While in a majority of patients you probably can use both technologies reasonably safely, there are factors that might lead to choosing one device over the other. For example, if a patient has very severe calcification of the annulus or the outflow tract, then our preference has been to use the self-expanding technology, mainly to avert a potential complication, which could occur with balloon-expandable technology: annular rupture or dissection of the annulus. During expansion, the balloon-expandable valve needs to over-expand to create a seal with the anatomy and overcome any potential recoil. In a calcified anatomy this can cause rupture or dissection, which is catastrophic for any patient, never mind high-risk, elderly patients. These complications have been reported, although fortunately not frequently, enough times for us to be concerned about using balloon-expandable valves in these types of patients.

A potential benefit of the balloon-expandable valve is that the requirement for contrast during the procedure generally has been lower compared with the self-expanding valves. This favours somebody who has really severe renal dysfunction where there is a risk of worsening renal failure due to contrast-induced nephropathy. However, patients with chronic renal dysfunction often tend to have quite calcified anatomy as well, so then you may have to switch back to the self-expanding where the risk of rupture is lower; we have to always balance the risk versus benefit.

At the annular level again, with the balloon-expanding technology, you have only one attempt at positioning the valve and, occasionally, there are patients who have borderline coronary ostia height with a real risk of coronary occlusion. In these high-risk patients, having a technology where you can position, have a look and retrieve again instantly if necessary increases the safety profile of the technology. Self-expanding, recapturable devices, such as Evolut R™ (Medtronic, Inc.), Portico (St. Jude Medical, Inc., USA) and the Lotus® valve (Boston Scientific, Massachusetts, USA), allow us to safely position the valve, check to see if the coronary ostia are perfusing and if they are, release the valve – if not, you can safely retrieve the device and look at another strategy. This cannot happen with the

balloon-expandable valve: you have to release the valve and hope for the best. Clinicians have tried various other techniques, such as protecting the coronary ostia with wires, but every time you put a catheter into a patient unnecessarily or for whatever reason, it always increases the potential for risk. Self-expanding recapturable technology has been a game-changer in terms of how we do TAVI, certainly locally but also globally.

Access is another big challenge for elderly patients with calcification. It is generally accepted the transfemoral approach provides better outcomes compared with the transapical access, although the patient risks are different. The self-expanding valves have the advantage that they have a much lower diameter than balloon-expandable valves after loading onto the delivery system. This really is a very important clinical feature that sometimes the companies have been a little shy in explaining to clinicians. You have heard of various terminologies – there are expandable sheaths or eSheath® (Edwards Lifesciences, Corp.), and these are, in general, sheaths that are able to expand once they have been inserted. This is profiled as a 14F (inside diameter [ID])/18F (outside diameter [OD]) or 16F (ID)/20F (OD), however, the eSheath expands to accommodate the valve and becomes 22.8F (OD) for the 23 mm, 24F (OD) for the 26 mm and >24F (OD) for the 29 mm Sapien 3 valves. For example, a 5.5 mm artery might need to be stretched up to 8.5 mm, which has the potential to increase the risk of vascular complications. That is something that is not always clearly understood when data have been presented. The Edwards valve is a balloon-expandable valve, and although a lot of work has been done in trying to reduce the sheath size and therefore protect the impact on vascular complications, the valve itself in its crimped form is about 19F to about 22–24F, so the body has to accommodate this valve once it has been inserted. The first-generation Medtronic CoreValve device was always 18F compatible. However, the new generation of CoreValve Evolut R™ has an integrated 'InLine' sheath and, thus, does not require a separate sheath, which reduces the delivery profile by about 4F. This means it is now truly comparable to advancing a 14F device into the patient's vessel. This is a significant change in terms of device profile. To date, we have only used Evolut R in a clinical trial platform but we have not encountered any difficulties using the Evolut R and advancing

the valve with the InLine sheath. However, as with any new technology, we will need to see how it transfers to a clinical environment, as more patients are treated with the device.

### Do smaller devices provide clinical benefits as well?

**GM:** This is an important point. The eSheath does allow you to advance the sheath via the femoral artery reasonably easily, but the eSheath and the artery will then need to expand to accommodate the larger valve and balloon. This forced expansion (going from 5.5 mm to 7.7 mm) has the potential to increase the risk of vascular complications.

Sometimes it is quite difficult to compare and contrast trial data using older-generation devices to current generation devices, because our techniques for patient selection have significantly changed and our understanding of what outcomes you will encounter by pushing hard with an oversized device have also changed. Historical studies use angiography to assess vascular size and all recent trials have used computed tomography (CT) to assess vascular size and access. While the overall rate of vascular complications is decreasing, regardless of the technology used, access will continue to be a very important feature that clinicians will use to decide which valve and implantation technique should be used. Ultimately, however, we all want a true lower-profile device, and an advanced sheathless platform, such as the Evolut R, will have the lowest-profile device to date in the market.

To this end, I do think the device companies should standardize the method in which valve profiles are labelled. It is my view that the all valves should be labelled by the outer diameter of its loaded or crimped form – this is the real diameter that the femoral artery and the patient will feel.

### How do self-expanding and balloon-expandable valves perform in terms of clinical outcomes?

**GM:** It is difficult to compare the two technologies as there is only one balloon-expanding device and probably seven or eight self-expanding devices. However, one thing is true for both types of devices: comparing the data with the new generation of both self-expanding and balloon-expandable technologies, the results are better than the historical results that we have seen.

One key difference, however, is the need for post TAVI pacemaker rate, which has been seen to be lower with the balloon-expandable device when compared with the self-expanding ones. Nevertheless, the pacemaker rate overall for the self-expanding is decreasing, as seen in several trials (Portico: 10.8%;<sup>1</sup> CoreValve US IDE high risk study: 19.8%<sup>2</sup>), predominantly driven by change in technique and more appropriate sizing using CT. We are now seeing pacemaker rates reduce down to the teens. It is likely that the Evolut R device, with repositionability, will enable better final valve positioning, potentially resulting in further reductions in pacing rates. The results of the Evolut R CE mark study has been submitted for publication - you will have to wait to read the results!

### Have there been any head-to-head studies that have compared the two types of device?

**GM:** There has been one head-to-head trial, the CHOICE study, which randomized Edwards XT against Medtronic CoreValve; however, this was a small study, without independent adjudication or corelab analysis, with a composite primary endpoint.<sup>3</sup> A high paravalvular leak drove the endpoint but this degree of leak was not observed in the large, CoreValve US IDE study, the first study to require use of CT sizing, which is not standard of care. More importantly, in the end, in CHOICE CoreValve showed trends toward better outcomes in stroke rate and similar mortality rates, which are accepted endpoints that matter most to physicians and their patients.

Bottom line, in terms of one type of valve against the other, all technologies appear to improve clinical outcome, partly due to improvements in techniques, partly due to improvement in patient selection. If you look at the overall EuroSCORE of the more recent trials compared with the first, early trials, the EuroSCORE has dropped by at least 3–5 points. These are still high-risk patients, but we are now getting better at identifying appropriate patients who will truly benefit from TAVI. Indeed, we have come to learn that there is a group of patients known as 'cohort C', where TAVI may not change the final outcome. With us moving away from these kind of patients, the 30-day mortality from all the recent, new-generation devices has been under 5%; some of them are even 2–3%,<sup>1,4,5</sup>

which is excellent when you consider that these are very high-risk patients. However, even established devices such as CoreValve have shown similarly low mortality rates (1.8% in ADVANCE II) in current practice.<sup>6</sup> That is a significant change in terms of important outcomes.

We all accept that the 'hard' outcomes such as mortality, although important, are at levels that would be deemed acceptable for the cohort of patients being treated. The things that I think we will be paying more attention to over the next few years are other markers of outcome, such as stroke, vascular complications, pacemaker implantation and, more importantly, paravalvular leakage (PVL). Certainly the US trials have suggested that the use of self-expanding valves has an immediate and, more importantly a progressive, long-term benefit in reducing PVL. The investigators found at 30 days the PVL rate was acceptable, and over 1 year that rate reduced further to levels that are consistent with next-generation valves on the market today.

### Are there any differences when you are carrying out the procedure in terms of ease of use, imaging or valve preparation?

**GM:** We do the procedure under local anaesthesia in over 90% of cases. We use general anaesthesia when patients require a surgical access. When we use local anaesthesia, we tend not to use echocardiography for deployment, but predominantly depend on fluoroscopy. The use of local anaesthesia, as long as it can be done safely and with similar outcomes, has the enormous benefit of reducing the cost and complexity of the procedure.

In terms of ease of use, both technologies are similar in terms of preparation, loading and delivering. The manufacturers have worked very hard to make it easier to load and prepare the valves on site. Our nurses have been trained to prepare and load any of the technology we will be using.

### With regards to TAVI devices, what will influence clinical decision making in the future?

**GM:** It will depend on probably a few factors: one would be the safety data, as cardiologists are very data-driven, so the data have to be favourable. The second factor will be ease of use, in that the device could be used via multiple access routes, delivered using the same technique and simple preparation methods – these will make a difference.

Repositionability will make a difference – a chance to redo the deployment will be beneficial and safer for the patient. The final factor is the cost. If you have two devices side-by-side and they both show somewhat similar pros and cons, then, cost will play a major role; none of us can avoid the significant funding issue with regards to TAVI.

### Are there studies ongoing that are going to provide helpful data that are going to influence clinicians' decisions or are further trials required?

**GM:** There are studies ongoing at present to assess the safety of TAVI in moderate-risk patients, as compared to surgery. The results of these studies have the potential to change how we treat moderate-risk patients with aortic stenosis. Another type of study that may be helpful is a device-versus-device study; however, one of the challenges of running a randomized trial today is that I think there are very few centres that are confident in using both technologies safely; thus the final outcome could be operator- and technique-related. In time, when more centres adopt another device and become competent, we should then be in a position to conduct a valid randomized valve-versus-valve study.

### What contribution has the education of physicians made to clinical practice?

**GM:** The TAVI manufacturers should be congratulated for this. They have taken a lead and have invested a lot of time and money in educating clinicians and their local representatives into imparting knowledge and advice in order to get good results. TAVI is one of the first devices where a great deal of investment has gone into the education of clinicians, users and ancillary staff, resulting in improved outcomes.

When we see ever-improving results with devices, a lot of it is, I believe, due to clinicians who are better at giving the right type of device to the right patients and who also have a better understanding of potential complications and solutions. I think, that has been more of an influence on outcome than the actual device type.

We, as clinicians, should do more to ensure that avoidable complications do not occur. Better patient assessments and case planning, using multiple access approaches, adherence to best practice and further innovations in technology

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should ensure better outcomes. We should be able to get these very high-risk patients to come out of the procedure in a safer manner, and we certainly need to improve on outcomes if the intention is to treat lower-risk patients with TAVI.

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REFERENCES:

1. Manoharan G. 2013. Presentation at TCT 2013.
2. Adams DH, et al. *NEJM* 2014;370(19):1790-8.
3. Abdel-Wahab M, et al. *Lancet* 2014;311(15):1503-14.
4. Meredith Am IT, et al. *J Am Coll Cardiol* 2014;64(13):1339-48.
5. Webb J, et al. *J Am Coll Cardiol* 2014;64(21):2235-43.
6. Petronio AS et al. Presentation at EuroPCR, 2014; Paris, France.

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