Ganesh Manoharan

TAVI optimisation: procedural improvements and expanding access to patients

Advances in first-generation transcatheter aortic valves have led to improved patient outcomes with the TAVI procedure. Current trials evaluating novel TAVI platforms and their use in low-risk patients, as well as ancillary devices, will likely continue to expand access to this therapy. *Confluence* spoke with Dr Ganesh Manoharan, Consultant Cardiologist at The Royal Victoria Hospital, Belfast, UK to discuss how this procedure is being optimised to reduce complications associated with treatment and expand access to a new patient cohort.

What is TAVI and how is it used to treat patients who require aortic valve replacement?

Dr Ganesh Manoharan (GM): TAVI is an acronym for 'transcatheter aortic valve implantation'; this is known as TAVR in the US, where the 'R' stands for 'replacement'. TAVI offers life-saving treatment for patients with severe symptomatic aortic stenosis, and is a viable alternative to traditional open heart surgery. However, almost 13 years ago, a Euro Heart Survey on valvular heart disease showed that approximately a third of patients who had severe symptomatic aortic stenosis were never actually treated, mainly because of age, case complexity, or challenges associated with open-heart surgery. TAVI has opened up a treatment option for a vast number of these high-risk patients.

The procedure started nearly 14 years ago, when the first valve was implanted by Prof. Alain Cribier in 2002.[1] Since then, there have been two large FDA-guided, randomised trials in the US, comparing TAVI versus open heart surgery for patients considered 'high-risk' or unsuitable for surgery. These trials used either the Edwards SAPIEN Transcatheter Heart Valve[2] or the Medtronic CoreValve®.[3] The Edwards SAPIEN trial[2] showed that TAVI was equivalent to open-heart surgery for patients with aortic stenosis, and the more recent Medtronic CoreValve trial[3] showed that TAVI was superior to open-heart surgery for treating patients with severe symptomatic aortic stenosis.

Since then, many registries in Europe have looked at TAVI. Overall, data show that TAVI is a very good and amenable way of treating symptomatic severe aortic stenosis for patients who are high-risk or surgically unsuitable. The global use of TAVI is rising exponentially and, as the procedure advances, complications and side effects continue to decline.

What does 'TAVI optimisation' mean to you?

GM: I think there are three areas for TAVI optimisation: patient selection, procedure improvements, and post-procedure planning and discharge. This is a very 'patient-centred' approach, rather than 'clinician-centred' or 'funding availability-centred'.

With regards to optimising patient selection, there are now quite a few ways of assessing frailty. Some trials underway are looking at using a more objective way to assess frailty and select patients for TAVI. Computerised tomography (CT) scans have helped patient selection on the basis of technical suitability; CT-guided imaging has been demonstrated to be the optimal way of assessing patients' technical suitability, both for sizing and access assessment. This allows us to better plan for a procedure in terms of transfemoral or alternative access approach. Furthermore, the use of 3D transoesophageal echocardiogram (TOE) has helped to evaluate patients that cannot undergo CT.

Advancement in technology has helped reduce TAVI procedural time and complication rates, and also allowed more patients to be treated via a transfemoral route. Resheathable technology

enables multiple attempts to optimise valve positioning, and going sheathless has allowed us to reduce the access site requirements. A minimalist approach to the TAVI procedure is also a means of optimisation, involving local anaesthesia without TOE guidance, angiography only, transthoracic echo only and use in fully conscious patients. This has enabled a more rational use of staff and resources. Patients then can be sent to a coronary care environment rather than to the intensive care unit (ICU), which helps promote early discharge. These methods have certainly improved the way we deal with patients in Belfast. Almost 80% of our patients are discharged within 48–72 hours post procedure, which is a huge saving in resources. Having a very clear discharge plan is important. We see patients at 30 to 60 days for an echocardiogram and then at 1 year post-discharge.

Another key factor to TAVI optimisation is investment from medical device companies in teaching and training. There is continued emphasis on optimisation, to make sure they get the best outcome with their devices.

How has TAVI been optimised in your centre?

GM: Here in Belfast, we optimised our TAVI approach very early, at the start of our programme in 2008. Our first patient was under full general anaesthesia and under TOE guidance. On the same day, our second patient was under local anaesthesia without TOE or general anaesthesia. Within 4 months we moved on to doing TAVI with no surgeon, bypass machine or anaesthetist in the room, but instead had all of these back-up facilities available within 5–10 minutes if required. We were the first centre in the world to do TAVI fully local, without any sedation. The first time I presented our local anaesthetic TAVI experience at a large meeting, I had some negative comments from the floor, but it is great to see that this type of approach is increasingly being adopted by many centres.

Today, almost 91% of our cases are done under full local anaesthesia. About 8% require either sedation or general anaesthesia because of alternative access approach or anxiety, for example. Using a local anaesthetic helps to mobilise patients quickly; we aim to have all patients sitting up and mobilising within 8–10 hours of TAVI, and certainly by the next morning. If they do not require any support, the vast majority are discharged within 48 hours.

As we have developed our service over the last 8 years, we have noticed big savings in resources. We now have the ability to do TAVI any day of the week, Monday to Friday, and we can do one or two cases every day. In 2008, we had 20 cases; last year we did 100. Despite an exponential increase in TAVI, the unit has coped very well without needing to open up any more beds or any more catheterisation (cath) lab slots.

What challenges are associated with optimising TAVI?

GM: We were fortunate to be a clinical trial site for Boston Scientific, Edwards, Medtronic, and St Jude Medical TAVI devices – so we had access to four different valve technologies and their individual distinct advantages. One of the challenges with trying to optimise TAVI is that not every centre will have access to all the different devices and the benefits these devices bring.

There may be institutional difficulties in trying to go fully local. It is sometimes very difficult to restructure your team and what I advise people to do then is not to remove your anaesthetist out from the room, but instead let them help you do the case in the way you normally do. There is no need to change the existing team structure when optimising the approach. The reality is, however, that the number of procedures will increase year on year, so optimisation will ultimately be necessary to save resources while maintaining safety.

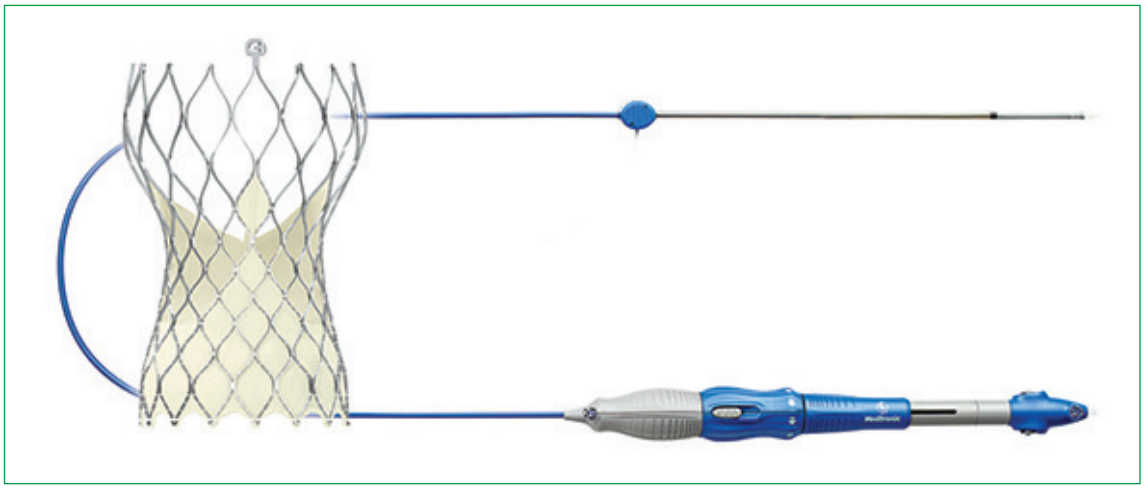
Additionally, the procedure is still expensive, and funding can be a serious issue, but commissioners have accepted that we are trying to do innovative work that has both reduced cost and optimised staff resources.

What technological advances had the most impact on TAVI optimisation?

GM: A key advance in technology is resheathability. Having a valve that is fully resheathable has infinitely improved patients' and clinicians' anxiety, because we know that we now have multiple attempts at getting TAVI right. Having a low-profile device and technologies that minimise side effects or complications, such as paravalvular leakage (PVL), stroke and the need for pacemakers, have all helped in delivering a minimalist approach. Reducing device profiles is important. The Corevalve® Evolut®R valve is the lowest profile device today, as it does not need an expandable sheath for delivery and has very low vascular complications (Figure 1).

fig. 1

CoreValve® Evolut® R



Every company I work with is improving their technology to make even the resheathable factor more reproducible. Ultimately, a device should be reproducible or predictably reproducible so that you know it will remain in place when fully released. All technologies are working on improving their seal to reduce PVL. This has helped optimise the procedure and has actually paved the way for more patients to be treated with TAVI, because if PVL was a major issue I am quite sure that the surgical fraternity would not be too open to dealing with moderate-risk patients.

What impact can transcatheter valve design have on paravalvular regurgitations?

GM: Predictable implant depth is important. PVL rates are compared from one device to another, but implant depths are not often reported. Each valve should be deployed according to the requirements of the instructions for use, in order to optimise its functionality. The CoreValve US trial and the SAPIEN trials have shown that if you deploy the device where it is intended to be, you get far superior results. We have seen that with Evolut®R and with Portico™. Additionally, having a skirt around the valve also improves PVL, as seen with SAPIEN 3 and Lotus™ valves. I expect that next generation devices will have iterations in all of those aspects and hopefully this will give us devices that are both compliant and predictable, and have almost no PVL complications.

How have changes in device technology affected the need for pacemaker implantation post-procedure?

GM: Traditional results suggest that self-expanding valves have a higher pacemaker implantation rate compared with balloon expandable devices. This has been seen in many trials, but, more recently, even the balloon expandable valves with a skirt, such as the SAPIEN 3, started having almost double the requirement for pacemakers when compared to the SAPIEN XT. When investigators looked at valve implant depth, it was clear this had a significant impact on the need to install a pacemaker.

Similar correlation between implant depth and the need for pacemaker was seen with newer self-expanding devices as well. If you deploy the valve no deeper than 6 mm sub-annular, you get a more predictable outcome in terms of need for a pacemaker.[4] We also found that this leads to more predictable PVL requirements, or lack of PVL, because you have the actual landing zone interacting with the annulus. Having the option of re-positioning should allow the clinician to optimise the final landing zone of the TAVI device.

What is the role of single or dual antiplatelet therapy in optimising TAVI?

GM: Data on using dual antiplatelet therapy post-TAVI is almost non-existent. It has been an experience-led strategy rather than a trial or data-led strategy. Traditionally, most patients would be put on aspirin and clopidogrel (Plavix®) for 1–3 months, unless they are having coronary stents, then they would be treated for up to 6 months. Very rarely, some patients even go up to 1 year. The challenge occurs when somebody is already on warfarin for other reasons, such as pulmonary embolism or atrial fibrillation. Do you just keep them on warfarin or do you add one antiplatelet or even three? Most centres do not put elderly high-risk patients on three different

agents (aspirin, Plavix® and warfarin). Traditionally, we would have kept them on aspirin and Plavix® until they are warfarinised and, once they are therapeutic, they go home taking only warfarin. If patients have already had a stent, then we keep them on aspirin and Plavix® post-stenting for 6–8 weeks and then offer them TAVI, so you are not confusing the burden of TAVI with the stent.

The introduction of new oral anticoagulants into TAVI is now being studied and, more recently, the issue of leaflet immobility has become a big challenge. We think this is triggered by thrombus formation on the leaflets and how we manage that is still being discussed and debated. The reassuring feature is that in all patients where leaflet immobility was observed, there have been no obvious clinical events or impact on valve function in terms of velocity or gradients. This is an area that is actively being studied.

What has led to lower-risk patients being offered TAVI?

GM: This change in treatment strategy is based on large trials, clinical experience and improving clinical outcomes. Both the PARTNER trial[2] and Medtronic CoreValve[3] trial studied high-risk patients. The PARTNER 2 trial,[5] which is the most recent large randomised trial, supports use of TAVI in intermediate-risk patients.

Over the years, patient selection has got better; patient assessments with CT guidance has increased and the technology has now advanced significantly from the first-generation devices. These factors have helped clinicians feel more comfortable with these procedures and get better and safer results.

The FDA has approved two technologies for trial in low-risk patients – SAPIEN 3 and Evolut®R. I think the results of these trials will dictate what happens to low-risk patients. I have no doubt that TAVI optimisation – patient selection, procedural outcome, post-procedure care and device improvements – has resulted in the FDA having the confidence to allow low-risk patient trials to start.

Clinical practice is often dictated by clinical trial results. I predict that the low-risk patients will actually have equal results to surgical aortic valve replacement patients, and that these patients will choose to have a minimally invasive approach to fixing their problem. That is what happened with percutaneous coronary intervention (PCI) and that is what will happen with TAVI as well. But the trial data have to reflect that the outcome from TAVI is, at worst, similar to surgery. I think patients will probably accept a marginal increase in the need for a pacemaker, but I do not think they will accept a marginal increase in death or stroke.

Are all TAVI devices equally positioned to provide the best treatment for low-risk patients?

GM: That is a difficult question to answer because there has been no trial looking at this, but I think that the devices that are being studied in low-risk patients must have the basics: a reproducible outcome, a predictable outcome with low PVL, a low pacemaker rate and low complication rates. If they meet these criteria, then they will meet the minimal requirements to be studied in low-risk patients.

Are there any areas of the TAVI procedure that should not be changed to ensure that outcomes are met in low-risk patients?

GM: The method of patient selection should not change: it should still be the responsibility of the heart team, especially as low-risk patients are traditionally surgical patients. I think the overall procedure should not change and should still be done by a team of experts. If you are a centre that is just starting TAVI today, then you should not be focusing on low-risk patients. Your remit should initially be high-risk patients for the first 3–5 years, so that the required skill-set and the post-procedure care are learnt.

For low-risk patients, the surgical team should be on-hand. If there is a left ventricle (LV) perforation, which still can occur regardless of the technology used, having a surgical 'bail out' within the first 5 minutes is important. One of the methods in our unit is to decide up-front, before the patient is even on the table, whether there is a bail-out strategy. In the low-risk patients, a bail-out strategy should always be there, and this will probably include having a cardio-thoracic team and bypass machine in the room.

What complications are expected from using TAVI in low-risk patients?

GM: TAVI has evolved in the opposite way to how coronary stents have evolved. PCI first started with the lowest-risk patients, whereas TAVI started out with the highest-risk patients. I am hoping that

when we perform TAVI on the lower-risk patients, all the potential complications we have seen in the high-risk patients will disappear, because usually the low-risk patients tend to have less calcification, they are more compliant, they tend to be younger and, therefore, the bundle conduction tissues are more robust. They have fewer comorbidities that can increase their risk of adverse outcomes, so what I am hoping is that low-risk patients will actually have fewer adverse events than high-risk patients. The precautions that we currently take with high-risk patients will still apply, but may not necessarily be needed.

How can the balance between safety and efficacy be resolved when optimising TAVI?

GM: Both go hand-in-hand. My biggest concern going forward is that the generation of interventional cardiologists who observed all the complications in the past will eventually retire, passing on the mantel to another generation of TAVI implanters who may not have experienced what their predecessors did. I hope the next generation will not take a lax approach to performing TAVI. This is where the device companies and meetings will become important foundations for educating new cardiologists in potential complications that were experienced years ago.

How do you see the use of TAVI changing in the short-term as well as the long-term?

GM: Short-term, if a centre is doing 50 procedures this year, they will be doing 150 in about 5–8 years. A lot of centres are seeing a massive rise in access to devices. Patients are living longer and aortic stenosis is almost synonymous with age. Patients' expectations will change with time and they will ask for TAVI rather than surgery.

Technology will continue to improve. Companies will try to ensure the procedure becomes as automated and predictable as possible, and they will continue to improve. A lot of the complications that we will see in future may not necessarily be due to the technology, but may be more related to the operator. That is why I think the emphasis on operator training and vigilance would become equally as important as what the technology can offer. I think we will end up routinely doing TAVI in moderate-risk patients with severe aortic stenosis, and low-risk patients will be eventually have equal access to TAVI in about 5–10 years.

Address for correspondence
Dr Ganesh Manoharan
The Royal Victoria Hospital
Belfast, UK

gmanoharan@msn.com

+44 28 90634123

REFERENCES:

1. Cribier A, et al. *J Am Coll Cardiol* 2006;47:1214–23.
2. Smith CR, et al. *N Engl J Med* 2011;364:2187–98.
3. Popma JJ, et al. *J Am Coll Cardiol* 2014;63:1972–81.
4. Manoharan G, et al. *JACC Cardiovasc Interv* 2015;8(10):1359–67.
5. Leon MB, et al. *N Engl J Med* 2016;374(17):1609–20.

DISCLOSURES: Consultant/Proctor for Medtronic, Boston Scientific, St Jude Medical