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Considerations in choice and evaluation of surgical and transcatheter aortic valves

In recent years, transcatheter aortic valve implantation (TAVI) has emerged as an alternative treatment option to surgical aortic valve replacement (SAVR). Historically, TAVI has been reserved for patients with a high surgical risk; however, increasingly, research has compared these two types of procedure in patients with lower levels of risk.

Confluence spoke with a surgeon, Mr Neil Moat, Consultant Cardiac Surgeon at the Royal Brompton Hospital, London, and an interventional cardiologist, Professor Helge Möllmann, Deputy Director of the Kerckhoff Heart Centre in Bad Nauheim, Germany, to discuss factors affecting valve choice and the evaluation of outcomes with these two different technologies.

In your Heart Team discussions, what criteria do you use to determine whether patients should be treated surgically or with transcatheter aortic valve implantation (TAVI)?

Neil Moat (NM): One needs to look at the factors that make the patients suitable or unsuitable for surgery or TAVI. In surgery, for example, we know that very elderly patients with a very low BMI have increased risk of mortality during surgery, and we know that patients with significant renal dysfunction have much higher mortality. There is a vast amount of experience with conventional cardiac surgery and markers of increased risk are fairly well defined. We have less experience with TAVI but I think that risk factors for paravalvular leak may include an aortic annulus that is too large for the largest size of valve, or a heavily calcified aortic valve with dense calcification. Access to the valve is another consideration for TAVI.

Helge Möllmann (HM): We start with a risk assessment, taking into account the patient's age and the risk as calculated by the EuroSCORE or Society of Thoracic Surgeons' (STS) score. This forms the basis on which we select patients for either TAVI or conventional valve replacement. There is however, a grey zone on either side of these rather strict age or score limits. Grey zone patients are discussed in great detail to decide which approach is most suitable for the individual.

NM: The Heart Team concept is vital for decision making about patients and in our institution it also involves heart failure and electrophysiology specialists. We also have a lot of input from care of the elderly physicians, and respiratory or renal physicians, as necessary. When you have an effective Heart Team it is very rare to see a lot of contention. The decision between TAVI and SAVR should come down to the Heart Team's clinical judgement, based on their investigations and discussions about the patient. It is very important for a number of people to meet the patient as this conveys an incredible amount of information to the group about the robustness of that patient.

How easy is it to define a patient's level of risk?

NM: Defining a patient's risk is not that easy. What one physician may mean by intermediate-risk may be very different to what another physician means, and I think individual patients have very different views too. These are the grey areas that Dr Möllmann mentioned, and a word of caution is that defining patients into these categories is not easy. The two main areas where debate arises are patients considered intermediate-risk for whom the group thinks there is no difference between TAVI and surgery, and the extreme-risk patients who may be too sick or too frail to benefit from any intervention. Of course, it would be nice to have tests or scores that would allow us to do this, but in reality we cannot predict outcomes for these groups by conventional scoring systems. We need to remember also that TAVI is not a terminal care; it is for people who are dying of aortic stenosis rather

than those dying with aortic stenosis. We can't just say 'Well, let's have a go doing a TAVI just in case.' I do not think that any healthcare economy can afford that type of thing, and it is probably not in the patient's best interest.

HM: Current European Society guidelines[1] suggests a EuroSCORE over 20 or STS score over 10, although I find these rather narrow margins. We end up with the sickest patients being treated by TAVI, and we have to question whether or not this is fair, because it is based on the assumption that surgical aortic valve replacement (SAVR) is always superior to TAVI. This means that younger and healthier patients are recommended for the conventional surgical approach, however I'm convinced that if we treated healthier patients with TAVI devices we would yield better results.

NM: Age is clearly a risk factor for conventional surgery but this is not definitive. You can have an 80-year-old patient who looks 65, or a 65-year-old patient who looks like they are 85. I think when we talk about risk, we need to extend the discussion to beyond mortality. Stroke is a complication that can have a big impact on a patient's life. Also, rate of recovery and the patient's ability to return home and lead a normal life are important outcomes; there are good data that TAVI performs better here. Minimally invasive surgical aortic valve replacement may reduce recovery times, although this does pose other potential issues, such as access.

What key clinical outcomes and valve characteristics influence selection of a surgical or transcatheter tissue valve?

HM: The problem is that SAVR and TAVI patients represent two completely different risk profiles that is either a consequence of age, or the procedure, but both do not necessarily correspond to each other. For this reason, completely different outcome measures apply to each approach. An important question with SAVR is whether or not the patient has a gradient afterwards, whereas with TAVI paravalvular leak or pacemaker implantation rate is much more of a concern. Most conventional surgical valves have an intra-annular design that yields gradients in the range of, say, 15 or 20 mmHg in patients with small anatomies. Implanting a TAVI device with a supra-annular design in these patients could easily achieve a gradient below 10 mmHg, representing an opportunity for intermediate-risk patients with small anatomy to be treated with TAVI and achieve good haemodynamic performance. Conversely, vascular complications are associated with TAVI, but not conventional surgery. I'm absolutely convinced that the rate of vascular complications could be decreased if we treated intermediate- or low-risk patients with TAVI, because those patients have healthier vessels, making the procedure much easier. For instance, pacemaker rate is around 5–6% with surgical aortic valves, but this is much higher with TAVI, for every system available. However, things are improving and pacemaker rates have already dropped from above 30% to 10–15%. With the new CoreValve Evolut R device (Medtronic, Inc., Minneapolis, MN, USA) (figure 1), together with more experience and improved implantation techniques, pacemaker rates will continue to fall. I'm sure that we can reduce the pacemaker rate below 10% for all devices within the next few years, at which point TAVI would be acceptable in lower-risk patients because outcomes will not differ much from SAVR.

NM: Short- and, indeed, long-term results following SAVR have been very, very good across the board in all countries. I think it is clear from some recent trials that the forward flow haemodynamics of the catheter-based valves are superior to those of stented bioprostheses, and are more akin to the favourable forward flow characteristics of stentless surgical bioprostheses.

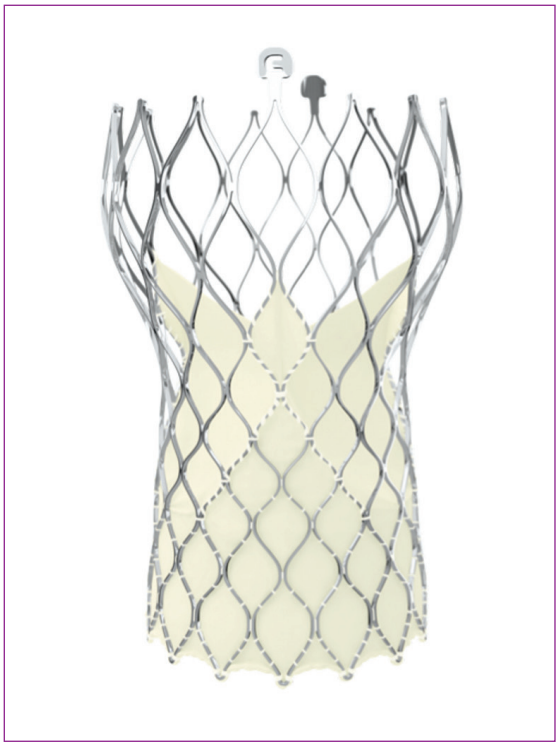

fig. 1
CoreValve Evolut R

There is no doubt that there has been an enormous shift towards the use of biological over mechanical valves, particularly in younger patients. Physicians and patients are thinking about what will happen in 8–14 years' time when that valve fails. If surgeons are using biological valves in younger patients, I think it is really important to implant a valve that retains the option for a successful TAVI valve-in-valve in the future, which means avoiding very small internal diameter valves. It is important for the surgeon to look at the size of the patient's annulus, and in patients who are likely to survive for longer than the valve they really need to implant a prosthesis that leaves the option for valve-in-valve TAVI in the future.

How much of a consideration is valve durability when deciding which treatment option is most suitable for a patient?

HM: At present, TAVI devices are predominantly intended for use in elderly patients, where longevity is not an important consideration. In contrast, in conventional surgery there is much more focus on how long the valve will last, because younger patients undergo SAVR. If we use TAVI in intermediate- or even low-risk patients, then we have to consider the question of how long the TAVI valve will function in that patient.

NM: Yes, the vast majority of patients who have been treated with TAVI in registries or trials have a mean age in the eighties, and we are not going to discover the answer to the question of TAVI valve durability from the patients who are currently being treated.

HM: I agree, we don't actually know how long TAVI devices last, because the longest experience is less than 10 years, much less than the experience we have with surgical valves. Of course, I hope that one day we will treat intermediate-risk patients with TAVI as well, and then the devices will have to achieve at least the same performance as surgical valves. In patients with an expected lifespan of 20 years or more, we cannot have a valve that lasts only 2 or 3 years and then needs replacement.

Do you expect that TAVI valves will last as long as surgical valves and that durability of those valves will continue to improve?

NM: That is a very interesting question, and I think one can only give a personal opinion as there are very few data. The only thing we do know is that the pulse duplicator testing of TAVI valves *in vitro* showed similar results to surgical valves.

There are some features of TAVI valves that might actually be associated with improved long-term durability over certain surgical designs. For example, in the surgical field there are increasing data to support the suggestion that stentless valves, such as the Freestyle® (Medtronic, Inc.), perform better in terms of durability than stented valves. One difference is that stentless valves have a much bigger orifice area and less energy loss across the valve, so implanting valves with more favourable forward flow haemodynamics might actually improve long-term durability. There are arguments one can put both ways.

My feeling is that, from the data with the first two valves that have been implanted in large numbers (SAPIEN series [Edwards Lifesciences, Irvine, CA, USA] and the CoreValve series [Medtronic Inc.]), there are no worrying early signs, but it will be some years before we can be sure that the valves will last, say, 10 years. There are examples, such as the St Jude Toronto valve (St Jude, Minneapolis, MN, USA), which looked very promising for about six and a half years, but then after seven and a half years it did not look good at all. I think it is going to be okay, but we have to watch and we have to be cautious.

What insights do the data from trials such as the CoreValve US trial, NOTION and PARTNER give us in terms of survival, haemodynamic outcomes, complications, and durability of surgical and TAVI valves? Have these data affected your practice or decision-making processes?

NM: The PARTNER[3] and the CoreValve US trial[2] enrolled high- to extreme-risk patients and I think it is quite clear that TAVI is at least equivalent to surgery in that population. You could argue, in terms of hospital stay, that TAVI is potentially superior to surgery based on the CoreValve trial data. The PARTNER trial was done very, very early in the experience with TAVI, and my suspicion is that if the trial was repeated now then the results in the TAVI arm would be significantly better than the original PARTNER data. I think, and I'm sure most people believe, that in very high- to extreme-risk patients, TAVI is probably superior to surgery.

Also of note is that the surgeons were quite constrained in these two trials and about half

of the patients in the surgical arms had stented bioprostheses with a label size of 19 or 21 implanted. These valves have a very small effective orifice area, and the PARTNER trial reported very high levels of patient/prosthesis mismatch in the surgical arms. I am just trying to raise a word of caution about whether the prescriptive nature of the surgery in such trials reflects real-world surgery.

HM: We also have to remember that NOTION[4] and PARTNER[3] are only very short trials, and even with the PARTNER data up to 5 years now, this is still much too short to speak about durability. All we can do is extrapolate from the data we have right now, and these data are really promising. We have excellent periprocedural outcomes and excellent hospital mortality outcomes. Even looking at long-term mortality, at least within the first couple of years, the results are promising. If we achieve a good result with the TAVI device with low paravalvular leakage, then the long-term result will most probably be at least as good as a SAVR.

The PARTNER SAPIEN3 trials[5,6] in intermediate-risk patients have shown an excellent result, but although these trials have the best scientific value, these patients may not necessarily reflect clinical practice as it is a controlled trial. However, NOTION has rather low-risk patients – it's more or less an all-comer trial, which nicely reflects daily clinical practice – and this is reassuring as it confirms that the way we are treating patients in clinical practice makes sense.

NM: While NOTION is an all-comers trial, the patients are still reasonably old. NOTION is a very commendable study, but it is very small. Another concern is that in the surgical arm, observed mortality was higher than the expected mortality calculated using the STS Risk Score. In almost every other study, including the two other trials mentioned, observed mortality is less than the expected or predicted mortality. Because of this, I think one has have to interpret NOTION with caution. It is likely that the result is not due to poor surgery, but a consequence of it being a small study and chance result. It will be very interesting to see the long-term follow up of the patients in NOTION, but it really is too small a study to answer many questions.

Following the data from the CoreValve US trial, NOTION and PARTNER, do we need to update the guidelines?

HM: The European guidelines were last updated in 2012,[1] and the expectation was that they would be updated again next year. My understanding is that that won't happen, and the next update of the aortic valve guidelines will probably be in 2017. In my opinion, that is much too late, because the 2012 guidelines are already outdated today.

Do you anticipate that TAVI will become a more viable option, or even the standard of care, for lower-risk patients?

HM: Definitely. I think the journey will go towards the intermediate- and low-risk patients. The problem is that the scientific rationale always takes a couple of years to impact daily clinical routine. Right now in Germany we treat patients with TAVI without evidence from a perfect scientific trial, but we are finding that this is the best way to treat them. The reality is that it takes at least 2 or 3 years before the clinical data appear. If I remember correctly, NOTION started to enrol patients in 2011. We are now 4 years down the line, and have much better devices and have already treated patients as they were treated in NOTION for 2 or 3 years.

What is needed is an all-comers trial in which all low- to intermediate-risk patients with aortic valve disease are randomised to either TAVI (transfemoral or transapical approach) or SAVR. This all-comers approach is vital to obtain scientific proof that can easily be translated into clinical practice. In the first PARTNER trials, the number of screened patients was in the thousands, but only a couple of hundred patients were enrolled. This definitely does not reflect what we see in daily clinical practice, so participating centres need to enrol all consecutive patients. In terms of outcomes, we need to see at least non-inferiority for TAVI devices, with a secondary analysis of TAVI superiority, at least in subgroups. I'm not convinced that non-inferiority of TAVI is enough, because SAVR costs a third of TAVI. From a social and economic point of view, we cannot opt for a much more expensive therapy that does not add additional value. We may not be able to demonstrate superiority in terms of survival, but quality of life and things like that play a role as well.

NM: In terms of a general clinical programme, some of the large national registries will be useful for tracking long-term outcomes following TAVI,

because many of the trials will not be funded to follow the patients for more than 5 years, and certainly all trials have their strengths and limitations. One of the great strengths of the UK TAVI Registry[7] is the capacity for long-term follow up. If these patients go on to die, that will be tracked; if they have an infarct, that will be tracked through the MI Registry; if they have a pacemaker later on, that will be tracked through the Pacemaker Registry; if they go on to have further surgery, that will be picked up. By linking these registries, we will be able to track these patients for very many years, and I think that will be a very useful resource.

What improvements do you still think need to be achieved in terms of TAVI compared with surgical valves?

HM: We have talked about pacemaker rates and about paravalvular leakage, and these need to be reduced or even abolished. Today paravalvular leak is less of a concern than even 2 to 3 years ago. As more centres start to offer TAVI, it is important that the procedure is very easy to perform, intuitive and safe. We should aim for systems that can be learned quickly and are forgiving if something goes wrong during the procedure. The easier and quicker the procedure itself is, the less anaesthesia support will be needed and this moves us towards a percutaneous coronary intervention (PCI)-like procedure. This move should be made with care, however, and does not imply that the Heart Team is no longer needed. Of course we still also have to take into account the vascular access. We are down to size 14 French catheters right now, which is very good, but perhaps we could aim for a system with even lower French sizes. These are the points we will be looking for the future.

NM: In the next 10 years both TAVI and SAVR will play an important role, and I think we need to understand which patients will do better with which technology. This will require a lot of work and a lot of understanding. If TAVI continues to achieve the promising results that it has so far, there will always be a big patient drive for minimally invasive procedures. Comparing PCI versus coronary surgery, a host of trials show that surgery has better outcomes, but most patients would still choose to have a PCI. I know many surgeons, myself included, who, if put in the place of a frail 79-year-old patient, would opt for TAVI even though surgery is the conventional treatment.

In younger or relatively low-risk patients, the problem will be cost. Surgery is a fairly cheap procedure whereas, if TAVI devices remain anywhere near their current price, there will be health economic pressures that may stop its growth in certain countries.

Do you think there is a need to provide more information on SAVR and TAVI options to cardiologists and GPs?

NM: I think there is. Going back only 5 or 6 years, we were really only testing the water with TAVI and trying to find out if it worked at all. Now there is a fairly general acceptance that TAVI is here to stay and is part of what I would call the standard armamentarium for treating patients with aortic valve disease. Once something has achieved that status, then people outside of the specialist centres need to know more about it to understand the pros and cons. I think that there is a need for a more systematic programme of education about TAVI. A lot of people have heard about it but really do not know enough about it – and this is not a criticism, but just reflects the relative newness of the technology.

HM: Education about TAVI is absolutely necessary because the media are still very sceptical about this new procedure. Therefore I think that GPs and patients should have access to better education about how easy and how safe the procedure is, and how good the results are today. We still struggle with results that were produced 5 years ago repeatedly appearing in TV reports, but we need to ensure that the very rapid developments that have taken place in recent years are made public.

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DISCLOSURES: NM is a Consultant to Medtronic and Tendyne. HM has received a speaker's honoraria or proctor fee from Abbott, Medtronic, St Jude Medical, Symetis.