TRANSCATHETER AORTIC VALVE IMPLANTATION: REVIEW OF CURRENT INDICATIONS, APPROACHES, FUTURE INSIGHTS, AND ALTERNATIVES

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ABSTRACT

The use of transcatheter aortic valve implantation is increasing worldwide, with rapid development of new generations of valves and the search for alternative access for implantation. The aim of this review is to summarise current approaches and indications, and to discuss some of the controversies surrounding this procedure.

Keywords: Transcatheter aortic valve implantation (TAVI), aortic stenosis (AS), review, aortic regurgitation (AR).

INTRODUCTION

Aortic stenosis (AS) is the most common heart valve disease in Europe and North America. Calcified AS occurs in 2–7% of the population >65 years old. The prognosis for untreated patients with symptomatic, severe AS is poor; the 5-year survival rate is between 15% and 50%.[1] The only effective and efficient treatment of symptomatic AS is valve replacement (Class I recommendation, Society of Cardiology [ESC] and the European Association for Cardio-Thoracic Surgery [EACTS] guidelines on the management of valvular heart disease, 2012).[2] Surgical aortic valve replacement (SAVR) still represents the gold standard among the therapeutic options for patients with severe symptomatic AS and low overall perioperative risk.[3] Young patients with low surgical risk undergoing SAVR have 30-day mortality rates as low as 0%, whereas elderly patients undergoing isolated SAVR have mortality rates up to 6.7% in patients aged 80–84 years and up to 11.7% in those aged >85 years.[4] Transcatheter aortic valve implantation (TAVI) has been developed as a minimally invasive alternative to open surgery, especially in patients with unacceptably high perioperative risk or patients who are not suitable for conventional surgery. The first implant in a human being was performed by Cribier in 2002[5] using a balloon expandable frame and an equine valve.

PATIENT SELECTION, INDICATION, AND CONTRAINDICATION FOR TRANSCATHETER AORTIC VALVE IMPLANTATION, AND PREOPERATIVE MANAGEMENT

TAVI indication is restricted to patients with severe symptomatic AS or degenerated bioprosthetic valves (currently off-label use) and excessive-risk related to open surgery. Operative mortality risk is mostly assessed using the European System for Cardiac Operative Risk Evaluation (EuroSCORE) and Society of Thoracic Surgeons (STS) risk scores (logistic EuroSCORE >20 or STS >10),

while taking into account risk factors that are not covered in the scores but are often seen in practice. The choice for TAVI is discussed by the institutional multidisciplinary heart team, typically consisting of interventional and imaging-specialists, cardiologists, cardiac surgeons, and anaesthesiologists. Patients are considered as suitable candidates for TAVI based on technical surgical reasons (e.g. previous cardiac surgery, calcified ascending aorta, or porcelain aorta not accessible for surgery) or because of a very high risk for a conventional operation (all reasons preventing the insertion of a catheter for external blood circulation, all conditions preventing aortic clamping, reasons preventing surgical access of the mediastinum such as the internal mammary artery or another critical conduit crossing the midline and/or adherent to the posterior table of the sternum, past history of mediastinal irradiation, burns, active mediastinitis). The absolute contraindications for TAVI are active or recent endocarditis or an annulus size that exceeds the recommendations of the valve manufacturers.[6]

The main results from the PARTNER trial in the cohort of patients with AS who were not suitable candidates for surgery can be summarised as follows.[7] First, standard medical therapy, including balloon aortic valvuloplasty, which was performed in 83.8% of the patients in the standard therapy group, did not alter the natural history of severe AS; at the end of 1 year, the rate of death from any cause was 50.7%, and the rate of death from cardiovascular causes was 44.6%. Second, transfemoral (TF) TAVI was superior to standard therapy, markedly reducing the rate of death from any cause (the primary endpoint), the rate of death from cardiovascular causes, and the rate of repeat hospitalisation. Third, the rate of death at 30 days among patients who underwent TAVI (5.0% in the intention-to-treat population, and 6.4% among patients who underwent TAVI) did not differ significantly from that among patients who received standard therapy in the cohort of patients who were not suitable candidates for surgery, despite the use of early-generation systems for TAVI and minimal operator experience with the TAVI procedure before the trial was initiated. Fourth, TAVI was also associated with a significant reduction in symptoms, as assessed with the use of the New York Heart Association (NYHA) classification system and the results of a 6-minute walk test. Fifth, there were more neurological events (including all strokes and major strokes), major vascular complications, and major bleeding events in the TAVI group than in the standard therapy group. Sixth, echocardiographic findings after TAVI indicated that the haemodynamic performance of the bioprosthetic valve was excellent and that there was no evidence of deterioration in the first year. TAVI was accompanied by the frequent occurrence of paravalvular regurgitation (PVR), which was usually mild, remained stable during the 1-year follow-up period, and rarely required further treatment for worsening symptoms.[7]

Experience with TAVI for severe aortic regurgitation (AR) is limited due to the risk of insufficient anchoring of the valve stent within the non-calcified aortic annulus. Absent or minimal calcification of native aortic cusps in pure AR result in the risk of insufficient anchoring and valve embolisation or residual PVR. Excessive oversizing carries a subsequent hazard for aortic root rupture or incomplete valve expansion.[8] Seiffert et al.[8] published their analysis on the initial German multicentre experience with the JenaValve™ (JenaValve Technology GmbH, Munich, Germany) transcatheter heart valve (THV) for the treatment of pure AR. Transapical (TA) TAVI with a JenaValve for the treatment of severe AR was performed in 31 patients (age: 73.8±9.1 years) in nine German centres. All patients were considered high-risk for surgery (logistic EuroSCORE: 23.6±14.5%) according to a local heart team consensus. Pure AR remains a challenging pathology for TAVI. After initial demonstration of feasibility, this multicentre experience provides broader evidence that the JenaValve THV is an adequate option in these specific patients due to its unique stent design and fixation mechanism. After the recent Conformité Européene (CE)-mark approval for this new indication in September 2013, patients with pure AR are being prospectively included in the currently recruiting JUPITER (Long-term Safety and Performance of the JenaValve) registry (NCT01598844).[8]

In all patients, preoperative multimodality imaging (transoesophageal echo cardiography [TOE], invasive cardiac evaluation with coronary, and supra-aortic angiography, left ventriculography, and multislice computed tomography [CT]) is usually performed to assess anatomic suitability, diameters of the aortic annulus and sizing of the prosthesis, distribution and amount of calcification, and aortic root geometry.

The degree of left ventricular (LV) hypertrophy, particularly upper septal hypertrophy and the angle between the aorta and the LV are important in planning the TAVI procedure. A septal bulge protruding into the LV outflow tract (LVOT) provides a challenge to the operator in the accurate placement of the valve and presents a significant risk of THV repositioning with cessation of the pacing run. LV dysfunction also influences the strategy of the procedure. For instance, in patients with severely depressed LV function, the number of pacing runs should be minimised to avoid haemodynamic compromise.[9]

Clinical endpoints and complications are defined according to the Valve Academic Research Consortium (VARC)-2 consensus criteria.[10] These include device success endpoints and safety endpoints (all-cause mortality, major stroke, periprocedural myocardial infarction, life-threatening bleeding, major vascular complications, and acute kidney injury), valve performance, and complications during hospitalisation at 30 days. A clinical efficacy composite endpoint after 30 days includes all-cause mortality, all stroke, and hospitalisation for valve-related symptoms, NYHA III or IV symptoms, or prosthesis dysfunction. VARC-2 also includes a new composite endpoint and time-related valve safety, which combines valve dysfunction, endocarditis, and thrombotic complications of the prosthesis.[10,11]

DEVICE DESCRIPTION

Currently, two devices are under post-marketing surveillance in Europe: the balloon-expandable Edwards SAPIEN© prosthesis (Edwards Lifesciences, Irvine, California, USA), which had the TF delivery system approved in November 2007 and the TA in January 2008, and the self-expandable CoreValve™ prosthesis (Medtronic, Minneapolis, Minnesota, USA), which was approved for commercial use in the European Union in May 2007.[12]

Edwards SAPIEN XT

This prosthesis is a second-generation device consisting of a bovine pericardial tissue valve in cobalt chromium. The frame height is designed to respect the surrounding cardiac anatomy and to minimise the risk of atrioventricular block, disruption of mitral valve function, and interference with coronary ostia. The Carpentier-Edwards ThermaFix process is intended to minimise the risk of calcification. The SAPIEN XT valve treats an annulus size ranging from 16–27 mm. All Edwards SAPIEN XT valve sizes are available for TF, TA, and transaortic (TAo) delivery. The SAPIEN XT valve may be used in the mitral position via the TA access route only.

The Edwards SAPIEN 3

This THV is a new-generation transcatheter bovine pericardial tissue valve. The polyethylene terephthalate outer skirt is designed to minimise paravalvular leakage and expand the annulus size coverage to 28 mm.[13]

The Medtronic CoreValve

The Medtronic CoreValve® is a porcine pericardial tissue valve, which provides controlled and accurate deployment via a self-expanding nitinol frame; it optimises the haemodynamics with supra-annular valve function, minimises paravalvular leakage with a conforming frame and a sealing skirt, and maintains coronary access. The new Evolut R CoreValve was initially launched with a 23 mm valve and is now expanded with the addition of 26 mm and 29 mm valves. Evolut R has the lowest delivery profile across all valve sizes through a 14 Fr equivalent system and is now indicated for minimum vessel diameters ≥5.0 mm. The CoreValve valve treats an annulus size range of 18–29 mm.[14]

The Third Lotus™ Aortic Valve Replacement System

Produced by Boston Scientific, this is a new fully repositionable device (bovine pericardium leaflets in nitinol frame) designed to facilitate more precise delivery by TF approach, and minimise PVR. The Lotus Valve System is designed to provide physicians increased control during implantation and to help provide a more precise, predictable procedure. It is the only aortic valve device that can be assessed in its final position prior to release, while maintaining the ability for the physician to reposition or fully resheath and retrieve the valve. The Lotus Valve System also incorporates a unique Adaptive Seal™ technology designed to minimise AR (leaking), a proven predictor of mortality. The Lotus Valve treats an annulus size range of 20–27 mm and is available in 23 mm, 25 mm, and 27 mm valve sizes.[15]

ACCESS

TAVI can be performed through several access approaches: TF, TAo, transcarotid, transaxillarian,

trans-subclavian (TS), and TA. In most centres performing TAVI, a TF first approach policy is applied.[11] In unsuitable peripheral arterial anatomy however, bleeding and vascular complications frequently occur and are associated with increased risk of perioperative morbidity and long-term mortality.[16]

Transfemoral Transcatheter Aortic Valve Implantation

The common femoral artery can be either prepared surgically or approached percutaneously. Echo-guided femoral access can be useful. Manipulation of the introductory sheaths should be careful and fluoroscopically guided. Depending on the size of the device, closure of the vascular access can be done surgically or by using a percutaneous closure device.

The femoral artery is typically used as the default vascular access. Peripheral vascular disease is not an absolute contraindication to TAVI; it does however increase the risk of complications significantly. Physicians must be skilled or have the necessary resources to treat vascular injuries (percutaneously or surgically). Alternatively, peripheral vascular interventions (percutaneous transluminal angioplasty or stent implantation) can be performed prior to valve implantation. Significant tortuosity alone of the iliofemoral vessels is not necessarily a contraindication to TAVI as long as the vessels are otherwise healthy, and compliant gentle advancement of the stiff guidewire or vascular access sheath will tend to straighten the vessel.[17] Contraindications of the TF approach are as follows: iliac arteries with severe calcification, tortuosity, a small diameter (<6–9 mm according to the device used), previous aortofemoral bypass; aorta: severe angulation, severe atheroma of the arch, coarctation, aneurysm of the abdominal aorta with protruding mural thrombus, the presence of bulky atherosclerosis of the ascending aorta and arch detected by TOE, and a transverse ascending aorta (balloon-expandable device).[2]

Transapical Transcatheter Aortic Valve Implantation

The TA approach is considered to be a more invasive and complex procedure.[18] It requires general anaesthesia but provides superior control of the valve positioning due to the shorter distance, potential reduction of stroke due to the absence of retrograde crossing of the aortic valve, and fewer access-site complications.[1] The TA approach is usually used when the patient is not suitable for the TF approach due to poor calibre iliac vessels or excessive tortuosity. The technique requires an anterolateral minithoracotomy, pericardiotomy, identification of the apex, and then puncture of the LV using a needle through purse string sutures. Subsequently, an introductory sheath is positioned in the LV, and the prosthesis is implanted using the anterograde route. Contraindications for the TA approach are as follows: previous surgery of the LV using a patch, such as the Dor procedure; calcified pericardium; severe respiratory insufficiency; and a non-reachable LV apex. There are currently no studies available directly comparing the TF and TA approaches.

Transaortic Transcatheter Aortic Valve Implantation

The TAo TAVI approach is preferred over the TA approach due to unsuitability of a lateral thoracotomy as a result of poor respiratory function, in addition to a forced expiratory volume in a 1 second/forced vital capacity (FEV1/FVC) ratio <70%; either the absolute value of FEV1 was <1 litre or FEV1 <60% of predicted and poor LV function i.e., <20% (to avoid LV puncture and repair).

The TAo TAVI procedure is performed through a J-shaped upper partial sternotomy, exposing the ascending aorta via a pericardial incision. Two pledged purse string sutures are placed at the selected spot, which is at least 5 cm from the aortic annulus and is free of calcification. After crossing the aortic valve using the Seldinger technique, the Ascendra© sheath is inserted into the ascending aorta. The valve is crimped on the delivery system in the opposite orientation.[19]

Subclavian/Axillary Transcatheter Aortic Valve Implantation

Currently, the alternatives to the femoral approach are the TA, the TS and the direct aortic access approaches. Petronio et al.[20,21] claim that the TS approach should be the first option to consider in patients with contraindications to the TF approach, but also in those patients who appear at higher risk of vascular complications in the case of a feasible but difficult TF approach. Although no direct comparison between the TS, TAo, and TA approaches is available, TS access should be favoured because of its lower invasiveness and its feasibility without general anaesthesia.

TS access was excluded in the case of vessel diameter of 6 mm, heavy calcifications, excessive tortuosity, and severe stenosis not amenable to balloon angioplasty. The presence of a permanent pacemaker (PPM) in the left pectoral region was not considered to be a contraindication, nor was the presence of a patent left internal mammary artery coronary graft, provided that the TS artery diameter was >7 mm.[20,21]

Transcaval Access (Caval-Aortic Access)

Caval-aortic access entails delivering large vascular sheaths into the abdominal aorta via the femoral vein through the inferior vena cava.[22] The rationale for caval-aortic access is that iliofemoral veins are larger and more compliant than corresponding arteries, the inferior vena cava is close to the abdominal aorta usually without interposed structures, and traumatic or aneurysmal aortocaval fistulae do not necessarily cause immediate haemodynamic compromise.[22] Greenbaum et al.[22] describe the first use of caval-aortic access and closure to enable transcatheter aortic valve replacement (TAVR) in patients who lacked other access options.[22] Between July 2013 and January 2014, 19 patients underwent TAVI via caval-aortic access.

Ott et al.[23] describe the first TAVI in Europe using caval-aortic access in a patient unsuitable for other access sites. They also report the first implantation of a SAPIEN 3 valve via caval-aortic access and the first use of an expandable eSheath during caval-aortic access.[23] Contrast enhanced CT was used to select a caval-aortic crossing trajectory with the least calcified aortic wall and no interposed structures, to determine suitable angiographic projection angles and fluoroscopic landmarks in relation to lumbar vertebrae. After puncture of the right femoral vein and the left femoral artery, aortic and caval angiography was performed simultaneously to identify the puncture site.[22] An Amplatz GooseNeck® Snare (ev3/Covidien, Dublin, Ireland) was placed in the aorta at the expected puncture site as a target to receive the wire used for crossing from the inferior caval vein. The crossing system consisted of an amputated stiff 0.014 inch guidewire (ASAHI™ Confianza PRO 9; Abbott Vascular, Santa Clara, CA, USA) inside a 0.035 inch wire converter (PiggyBack™; Vascular Solutions, Minneapolis, MN, USA) inside a support catheter (NaviCross®; Terumo, Somerset, NJ, USA) inside a guiding catheter (RDC1™; Cordis Corp., Fremont, CA, USA).[22,23] Crossing was performed during a 2-second application of 50 W to the distal guidewire using electrocautery to vaporise surrounding tissue. The guidewire was then captured by the snare and placed in the thoracic aorta. Subsequently, the crossing system was replaced by a rigid 0.035 inch guidewire (Back-Up Meier™; Boston Scientific Europe, Ratingen, Germany) and a 14 Fr, 35 cm long Edwards TAVI expandable introducer sheath (eSheath©; Edwards Lifesciences, Irvine, CA, USA) was slid from the femoral vein, inferior caval vein, through the caval-aortic tract into the abdominal aorta without dilatation. TAVI was then performed according to the standard protocol. The caval-aortic junction was then closed with a 6 mm AMPLATZER™ Muscular VSD Occluder (St. Jude Medical, St. Paul, MN, USA) using an 8.5 Fr Agilis™ deflecting sheath (St. Jude Medical) inside the TAVI sheath. Device size was selected to approximate the outer diameter of the sheath (8 mm max diameter during passing of the crimped transcatheter valve) assuming some degree of recoil of the eSheath and the distance between the aorta and the caval vein. The occluder was deployed by exposing the distal disc in the aorta, retracting to apply to the aortic wall and deploying the proximal device near the caval vein. Aortography was performed to ensure no retroperitoneal accumulation of contrast media. Protamine was applied to reverse heparin anticoagulation. The femoral vein access site was closed using two prepositioned sutures (ProGlide®; Abbott Vascular).[22,23]

DISCUSSION

The prognosis in symptomatic patients with severe AS is poor if treated medically. After symptoms onset, the 1-year mortality rate is reported to be around 30%.[24] TAVI was accepted as a minimally invasive alternative to open surgery for patients who are not suitable for conventional surgery. The 2-year follow-up of patients in the PARTNER trial supports the use of TAVI as an alternative to surgery in selected high-risk patients with aortic stenosis. The two treatments were similar with respect to mortality, reduction in cardiac symptoms, and improved valve haemodynamics. The early increase in the risk of stroke with TAVI was attenuated over time. A new, important observation was the association of PVR after TAVI with late mortality. Work should now be directed toward reducing paravalvular AR with improved

device designs, techniques for more precise valve sizing and positioning, and judicious use of post-TAVI dilation.[25] The TF approach is the preferred first choice of access, because it can be carried out completely percutaneously and without any general anaesthesia. TA patients usually have a higher estimated preoperative risk prediction and higher incidence of comorbidities. The literature offers only limited information which directly compares TF TAVI and second most often using TA TAVI. The UK TAVI Registry was established to report the outcomes of all TAVI procedures performed within the UK. Data were collected prospectively on 870 patients undergoing 877 TAVI procedures between January 2007 and December 2009. Follow-up ranged from 11–46 months. The majority (69%) of implants were by the TF route. The remaining (31%) of implants were performed as non-TF. The majority (>85%) of non-TF approach cases were done via the TA approach. In this cohort of patients the 30-day mortality was 7.1%, which is comparable to that reported in previous registries: the SOURCE (SAPIEN Aortic Bioprosthesis European Outcome) registry, 8.5%; FRANCE (French Aortic National CoreValve and Edwards) registry, 12.7%; the German registry, 8.2%; and the Italian registry, 5.4%. There was higher 30-day mortality among patients receiving a non-TF implant compared with patients receiving a TF TAVI (p=0.03). The explanation is probably multifactorial, the non-TF cohort of patients has a more adverse risk profile, but it is also possible that aspects of the TA procedure may confer an increased risk.[15]

Our reasons for a 'clear TA approach' strategy for all high-risk patients considered as candidates for TAVI are the more precise control, the deployment of the valve in the correct position, and the better and more intuitive manipulation of the device at a shorter distance. In recent patients we decided to perform angiography during the valve deployment while inflating the balloon, as described by Pasic et al.[26] as part of 'the Berlin addition'. Angiography enabled perfect visualisation of the position of the prosthetic valve and its relationship to the coronary arteries, aortic valve annulus, and valve cusps throughout the valve deployment. Angiographic visualisation improves the safety of TA TAVI and simplifies valve positioning and the valve-deploying technique.[26] Also, the TA approach is independent of the degree of the patient's peripheral artery disease, calcification, diameter, and other anatomical variables of the inguinal and iliac vessels.

Mitral regurgitation (MR) is present in most patients with severe AS. Consequently, little is known about the impact of MR on clinical outcomes after TAVR and the impact of TAVR on MR.[27] A Canadian registry reported that severe MR was present in 17% of patients who died ≤30 days after TAVR but only 7% of those who survived. The Italian CoreValve registry reported that Grade 3 or 4 MR was present in 13.2% of patients who died but only 4.9% of those who survived at a median of 69 days after the procedure (hazard ratio: 4.62).[27] Interesting data arose from the PARTNER (Placement of Aortic Transcatheter Valves) studies suggesting that patients with moderate or severe MR may derive a large benefit from TAVR compared with both medical management and SAVR.[27] In the PARTNER B study, subgroup analysis showed that the number needed to treat to prevent one death at 1-year was three in patients with moderate or severe MR, compared with seven in patients without. In the PARTNER A study, 1-year mortality of patients with moderate or severe MR was 24.2% after TAVR and as high as 35% after SAVR.[27] Little information is available with regard to changes in MR after TAVR. Durst et al.[28] reported an improvement in mild-to-moderate MR after TAVR with the SAPIEN valve in 12 of 35 patients (34%). The absence of mitral annular calcification was associated with improved MR.[28] Tzikas et al.[29] reported a reduction in moderate-to-severe MR after TAVR with the CoreValve prosthesis, improving in six of ten patients (60%), remaining unchanged in three patients (30%), and worsening in one patient (10%).

Today, a shift towards lower-risk patients is currently taking place. At this time, two clinical trials are currently recruiting intermediate-risk patients to directly compare the outcomes of patients undergoing SAVR or TAVI. The PARTNER II trial randomly assigns patients at intermediate surgical risk to undergo either SAVR or TAVI with the Edwards Sapien XT bioprosthesis (ClinicalTrials.gov identifier: NCT01314313).[4] The main results from the PARTNER 2 cohort A randomised trial involving intermediate-risk patients can be summarised as follows.[30] First, TAVR, performed in experienced centres, with the use of a lower profile, next-generation device, was non-inferior to surgery with respect to outcomes at 2 years (death from any cause or disabling stroke). Second, bioprosthetic valve gradients were lower and the areas were greater with the SAPIEN XT valve, as compared with surgical valves, whereas

the incidence of paravalvular AR was higher after TAVR than after surgery. Third, several benefits with regard to secondary endpoints were associated with TAVR, including lower risks of bleeding events, acute kidney injury, and new-onset atrial fibrillation, as well as more rapid early recovery that resulted in shorter durations of stay in the intensive care unit and hospital. The possible superiority of TAVR over surgery in the TF access cohort is a new finding for balloon-expandable transcatheter valves. It requires prospective evaluation in a suitably powered superiority study.[30] In addition, a SURTAVI trial is presently recruiting intermediate-risk patients to undergo treatment by SAVR or TAVI with the Medtronic CoreValve bioprosthesis; this will provide additional important information regarding this issue.[4]

New devices, such as sutureless valves, will also be adopted in daily practice and taken into account during the decision-making process, especially in lower or intermediate-risk patients. A sutureless aortic bioprosthesis represents a new generation of bioprosthesis, another therapeutic option in the spectrum of aortic valve replacement, and the second most important advance in the treatment of aortic valve diseases in recent years, after TAVI. They combine the advantages of stentless valves in terms of haemodynamic parameters (a more efficient effective orifice area) and simple and safe implantation. Similar to conventional surgical replacement of the valve, sutureless bioprosthesis requires valve excision (a risk reduction of paravalvular insufficiency compared with TAVI) and annular decalcification, but permanent fixation sutures are not required.[31] The possibility of avoiding suture placement and their tidying may lead to shorter procedural times.[24,32] The potential to reduce operative time may be beneficial in high or intermediate-risk patients. The construction of this valve also supports minimally invasive approaches in cardiac surgery (insertion through the partial sternotomy or right thoracotomy). These advantages could be of benefit to patients who have no fundamental contraindications for using cardiopulmonary bypass and are undergoing complex, combined procedures or re-operations. Patients with a small aortic annulus or heavy calcification of the annulus and aortic root, where positioning sutures may represent technical problems and complications, are another potential group that could benefit. It is important to also take into account the economic aspect of using transcatheter or sutureless valves in lower-risk and younger patients. There are some potential future situations that any interventionist should be aware of, such as development of ischaemic heart disease in younger patients and complicated access for coronary angioplasty through the valve frame.

The most commonly reported complication after TAVI which affects long-term outcomes is PVR, stroke, and PPM implantation. The reported rates of moderate or severe regurgitation during the TAVI procedure vary from 10–20% or more in larger series, regardless of the type of prosthesis.[24] Regurgitation after TAVI is known to have a negative impact on mid and long-term survival.[33] Unbehaun et al.[34] reported mild-to-moderate regurgitation in 20% of patients. Results from the Italian Registry of TA TAVI showed that 45% of patients had mild or moderate AR at hospital discharge.[35] O'Sullivan et al.[36] summarised in their work that there are two anatomical, non-modifiable factors, which have an impact on the likelihood of PVR: aortic valve calcification and calcium distribution, and LVOT aortic valve angle. There are two other valve-related, modifiable factors that determine the incidence of PVR: prosthesis-annulus incongruence and valve position.[36] PVR occurrence in the future will probably decrease with several improvements in valve designs ('skirts' to seal the aortic annulus), deployment techniques, and operator skills.

Patients undergoing TAVI are also at high risk of both bleeding and stroke complications, and specific mechanical aspects of the procedure itself can increase the risk of these complications (retrograde passing through the aortic arch and aortic valve and operator experience).[37] The mechanisms of peri-procedural bleeding complications seem to relate mainly to vascular/access site complications (related to the use of large catheters in a very old and frail elderly population), whereas the pathophysiology of cerebrovascular events remains largely unknown.[37] Several cerebral protective devices have been developed to decrease the incidence of this complication.

Antithrombotic therapy in the setting of TAVI has been empirically determined, and unfractionated heparin during the procedure followed by dual antiplatelet therapy (DAPT) with aspirin (indefinitely) and clopidogrel (1–6 months) is the

most commonly recommended treatment.[37] However, bleeding and cerebrovascular events are common; these may be modifiable with optimisation of peri-procedural and post-procedural pharmacology. In the PARTNER trials, procedural parenteral anticoagulation therapy consisted of a 5,000 IU bolus of unfractionated heparin followed by additional boluses to maintain an activated clotting time of 250 secs. Recently, the American College of Cardiology Foundation/American Association for Thoracic Surgery/Society for Cardiovascular Angiography and Interventions/Society of Thoracic Surgeons (ACCF/AATS/SCAI/STS) expert consensus document on TAVI recommended maintenance of an activated clotting time >300 secs.[25] This document also stated that heparin anticoagulation could be reversed by administration of protamine sulfate at a milligram-to-milligram neutralisation dose. After TAVI, DAPT with aspirin (80–325 mg daily) and clopidogrel (75 mg daily) has been used in most centres and studies. However, the use of a loading dose of clopidogrel (300–600 mg) before TAVI is usually not specified, and the duration of clopidogrel therapy has varied widely among studies (usually 1–6 months). In the PARTNER trial, the recommendation was to use aspirin (75–100 mg per day) for life and clopidogrel (75 mg per day) for 6 months, with a 300 mg loading dose if the patient was not already taking clopidogrel.[7] The ACCF/AATS/SCAI/STS panel recommends DAPT with aspirin and clopidogrel after TAVI to reduce the risk of thrombotic or thromboembolic events, but its duration and the use of a loading dose of clopidogrel are not specified.[38] About one-third of patients undergoing TAVI will already be receiving an oral anticoagulant, typically warfarin for chronic atrial fibrillation. For these patients, there has been a lack of uniformity regarding the choice of post-procedural antithrombotic treatment. They have, therefore, received either triple antithrombotic therapy (warfarin with aspirin and clopidogrel), warfarin with one antiplatelet drug (aspirin or clopidogrel), or warfarin alone after TAVI, at their physicians' discretion. There are currently no data on the use of new anticoagulants, such as the direct thrombin or factor Xa inhibitors, in this population. In the PARTNER trial, there was no specific recommendation for either the peri-procedural or later anticoagulation management of this increasingly prevalent patient population. The ACCF/AATS/SCAI/STS expert consensus recommends that low-dose aspirin be continued, but that other antiplatelet therapy should be avoided whenever possible. The use of triple antithrombotic therapy is likewise discouraged in the Canadian Cardiovascular Society (CCS) statement on TAVI.[38]

Cardiac conduction abnormalities occurring after SAVR result in a 1–8% requirement of a PPM. This complication can be explained by the close proximity of the operative procedures to the sinoatrial node and atrioventricular node, which can result in trauma to the conduction system, and the presence of coronary artery disease, which leads to ischaemic injury.[39] The incidence of PPM implantation after TAVI using the CoreValve device has been reported to be in the range of 20–39%. In studies where the Edwards SAPIEN valve was used, the incidence of PPM implantation has been reported in the range of 5–12%. The explanation of the higher incidence of PPM implantation after TAVI includes patient factors such as comorbidities, mechanical trauma to the conduction system during procedures, valve oversizing, and valve design, especially in the self-expanding design of the CoreValve, which contains a subannular skirt that is typically placed 4–8 mm below the aortic annulus and expands in the LVOT.[39]

CONCLUSION

TAVI became a very attractive, safe, and effective therapeutic option which can be performed with an acceptable mortality rate in selective high-risk patients. TAVI today is not limited to inoperable or high-risk patients only. Currently, there is a trend toward shifting the indication towards lower-risk and younger patients, and to expand the current use of transcatheter aortic valves outside the manufacturer recommendations, mainly as a valve-in-valve procedure for degenerated aortic or mitral valve bioprostheses and TAVI in pure AR for high surgical risk patients.

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