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Development of Transcatheter Aortic Valve Implantation and its Clinical Implications

Sofia Metaxa, MD

First Department of Cardiology, Evagelismos Hospital, Athens, Greece

In the early 1990s the concept of transcatheter aortic valve implantation (TAVI) appeared challenging and totally unrealistic. It was a true "resurrection" for Cribier and his whole team[1] performing the first TAVI in an inoperable patient in 2002, using a transeptal antegrade approach and balloon-expandable aortic valve prosthesis. Since then TAVI has been performed in more than 50000 patients worldwide. TAVI is currently indicated in patients with severe symptomatic aortic stenosis (AS) and acceptable life expectancy who are not suitable for aortic valve replacement (AVR) (indication class IB) or as an alternative to aortic valve replacement (AVR) in selected high-risk operable patients (class IIB), according to the "Heart Team" assessment.[2]

The TAVI Heart Team comprised of clinical cardiologists, interventionalists, surgeons, anaesthetists and imaging specialists with expertise in the treatment of valve disease, selects patients suitable for TAVI taking into account advantages and disadvantages of both AVR and TAVI. A logistic EuroSCORE ≥20% (logistic EuroSCORE I tends to overestimate observed mortality risk by a factor of 2 to 3 and a newly updated logistic EuroSCORE II is currently available in clinical practice) or a Society of Thoracic Surgeons (STS) score >10% are suggested as indications for TAVI therapy.[3] Recent publications have identified a number of baseline variables independently associated with mortality or poor outcome in patients undergoing TAVI (low body mass, functional status, left ventricular dysfunction, NT-proBNP, prior stroke, diabetes, chronic kidney disease, anemia, severe tricuspid and mitral regurgitation, porcelain aorta or history of chest radiation) which could be integrated into new scoring systems to quantify and predict the prognosis of TAVI both in the immediate and in the long term (Table 1).[4] Apart from certain absolute and relative contraindications for TAVI (Table 2)[2] a number of subgroups require more precise evaluation, for example transcatheter 'valve in a valve' appears as an attractive alternative in bioprosthesis failure with more than 100 successful TAV-in-surgical aortic valve procedures already been performed.[5,6] Several successful case reports document stenotic bicuspid aortic valves been treated with TAVI and according to a German

registry, 16% of patients with intermediate risk of surgery for AS have chosen TAVI as a therapeutic regimen.[7]

The most important aspect of anatomical screening involves assessment of arterial vasculature and aortic valve complex to guide access route (transfemoral, transapical, subclavian or direct aortic) and transcatheter valve size.[3] Peripheral contrast angiography is practical and associated with relatively lower costs and lower radiation or contrast exposure compared with multislice computed tomography (MSCT), which provides more precise information regarding vessel size, tortuosity and calcific burden. Typically the femoral artery is used for vascular access and vascular injuries are treated "on the way out" by percutaneous transluminal angioplasty, stent implantation or surgery.

The aortic valve complex (left ventricular outflow tract, aortic annulus, sinus of Valsalva, sinotubular junction and ascending aorta) can be measured by different imaging modalities including echocardiography (transthoracic, transesophageal or 3D), aortography, MSCT and magnetic resonance imaging. Due to a non-circular shape of the aortic valve annulus it is difficult to find the proper sizing of the transcatheter aortic bioprostheses and routinely the implanted valves are oversized to limit aortic regurgitation and obtain procedural success.[7] Currently two valve models are available: the Edwards SAPIEN valve and the Medtronic CoreValve. The Edwards SAPIEN valve consists of tri-leaflet bovine-pericardium valve mounted on a balloon-expandable stainless steel stent, is available in four sizes (20, 23, 26 and 29 mm) and can be implanted in native annuli with diameters of 16 to 27 mm. The CoreValve has an autoexpandable nitinol stent containing a porcine pericardial valve, is available in three sizes (26, 29 and 31 mm) and can be implanted in native annuli ranging from 20 to 29 mm.[1,3]

Optimal management of patients undergoing TAVI includes resolving a vast variety of issues and constantly improving valves and delivering systems. According to published case series, up to three quarters of TAVI patients have coronary artery disease and percutaneous coronary intervention (PCI) is reported in up to 44% of them, safely performed in addition to TAVI either as a staged or a concomitant intervention.[8] Stroke has been highlighted as an important problem after TAVI: most periprocedural and postprocedural strokes are of embolic origin (new cerebral lesions have been reported in 58 to 91% of patients undergoing TAVI)[9] and studies are ongoing to establish the proper therapeutic regimen including embolic protection devices and dual antiplatelet therapy. Complete heart block is frequently reported after TAVI because transcatheter valves are implanted lower into the left ventricular outflow tract against the interventricular septum. Treating TAVI patients with improved delivery systems will ameliorate valve positioning and decrease the incidence of this complication as well; rate of new pacemaker implantation reaches 9-36% with the CoreValve and 3-12% with the Edwards device.[10]

Several large registries have been published showing excellent short- and mid- term results after TAVI using both the transfemoral (TF) and the transapical (TA) access route. The SOURCE registry enrolled 1038 patients at 32 European centers, treated with an Edwards SAPIEN valve either by TF (n=463) or TA (n=575) approach; procedural success was 95.2% and 92.7%, 30-day mortality was 6.3% and 10.3%, and 1-year survival was 72.1% and 81.1%, respectively.[11] The ADVANCE registry included 1015 patients with mean logistic EuroSCORE 19.2% and measured cardiovascular/all-cause mortality at 30 days (3.4/ 4.5%), 6 months (8.4 / 12.8%) and 1 year (11.8 / 17.9%) respectively.[12] In 2011 four mixed national registries showed 1-year survival rate ranging between 71.9 to 81.6% and 2-year survival rate 73.7%[7] and the recent FRANC 2 registry reported procedural success rate 96.9% and 1-year survival 76%.[13]

While registries contribute to better appraisal of patient screening, improvements in technical modalities and better management of complications in the 'real world' of TAVI, more rigorous assessments are available from the first multicentre, randomized clinical PARTNER Trial (Placement of Aortic Transcatheter Valves). At first, a total of 358 patients with inoperable aortic stenosis underwent randomization (TAVI versus standard therapy, including balloon aortic valvuloplasty) and it was found that at 1 year, TAVI resulted in reduced rates of death from any cause (30.7% in the TAVI group vs 50.7% in standard therapy, P<0.001), composite end point of death or repeat hospitalization and cardiac symptoms, despite a higher incidence of major strokes and vascular events.[14] Survival advantage associated with TAVI remained significant at 2 years of follow-up; rate of deaths 43.3% in the TAVI group and 68% in the standard therapy group (P<0.001) – cardiac mortality 31% and 62.4% respectively (P<0.001). Moreover, in the TAVI group rehospitalizations were less, functional status and echocardiographic findings remained improved at 2 years.[15]

The PARTNER cohort A compared TAVI with AVR and met its non-inferiority endpoint; the all-cause mortality was 3.4% in the TAVI group and 6.5% in the AVR group at 30 days (P=0.07) and, at 1 year 24.2%

versus 26.8% respectively (P=0.44). At 30 days major vascular complications were significantly more frequent with TAVI (11% versus 3.2%, P<0.001), while major bleeding (9.3% versus 19.5%, P<0.001) and new-onset atrial fibrillation (8.6% versus 16%) were more frequent in AVR.[16] Most recently, a 2-year follow up of patients in the PARTNER Trial has been published supporting TAVI as an alternative to AVR in high-risk patients. It was found that all-cause mortality (33.9% in the TAVI group, 35% in the AVR group, P=0.78) and cardiovascular mortality (21.4% in the TAVI group, 20.5% in the AVR group, P=0.80) at 2-years were similar in both groups and most importantly, the frequency of all strokes during follow up did not differ either (P=0.52). Both treatments were found similar with respect to mortality, reduction in symptoms and improved valve hemodynamics but paravalvular regurgitation was more frequent after TAVI (P<0.001) and was associated with increased late mortality (P<0.001).[17]

Subanalysis of the PARTNET cohort A regarding health status and quality of life in high-risk patients with severe AS demonstrated substantially improved health status with TAVI at 1 month (via the TF but not the TA route) and similar findings for both TAVI/AVR at 6 and 12 months.[18] TAVI has been shown to be superior to standard medical therapy resulting in ameliorated quality of life with mean cost $42806 for the initial procedure and $78542 for the whole hospitalization, but reduced hospitalization rates through the first year of follow-up make TAVI an economically attractive strategy.[19] Although 12-month costs and quality-adjusted life-years (QALY) were found similar for TAVI and AVR in the overall population of PARTNER cohort A, total 12-month costs were slightly lower and QALYs were higher for patients undergoing TAVI via the TF route (results for the TA cohort were economically unfavorable); nevertheless, additional studies are needed to establish TAVI a cost-effective therapeutic regimen.[20] Finally, the PARTNER Stroke Substudy analyzed all neurologic events (transient ischemic attacks and strokes) of patients treated with either TAVI or AVR and concluded that neurologic complications occurred more frequently after TAVI in the early phase but thereafter, the risk was influenced by patient- and disease-related factors (e.g. history of recent stroke or transient ischemic attack, advanced functional disability).[21]

Table 1. Predictors of long-term mortality after TAVI[4]

Advanced age
Smoking
Logistic EuroSCORE
STS Score
Calcium Score
Baseline anemia
Baseline renal failure, acute kidney injury
Pulmonary hypertension
COPD
Liver disease
Prior stroke
Major vascular complication
Myocardial injury
Systematic inflammatory response syndrome
Learning curve, early experience with TAVI

COPD = chronic obstructive pulmonary disease; TAVI = transcatheter aortic valve implantation

Table 2. Contraindications for transcatheter aortic valve implantation[2]

Absolute contraindications	**Life expectancy < 1 year** **Major comorbidities resulting in minor improvement of quality of life** **Disease of other valves with need for surgical treatment** **Inadequate annulus size (< 18mm/ >29 mm)** **Thrombus in LV** **Active endocarditis** **Elevated risk of coronary ostium obstruction due to anatomical characteristics** **Plaques with mobile thrombi in the ascending aorta or arch** **For transfemoral/subclavian approach: inadequate vascular access (vessel size, calcification, tortuosity)**
Relative contraindications	**Bicuspid or non calcified valves** **CAD requiring revascularization** **Hemodynamic instability** **LV ejection fraction <20%** **For transapical approach: severe pulmonary disease, LV apex not accessible**

CAD = coronary artery disease; LV = left ventric-le(-ular)

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