REVIEW ARTICLE

Transcatheter Aortic Valve Implantation: Where are we in 2020?

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Abstract

Aortic stenosis is an insidious disease of rapid progression after the onset of symptoms. Aortic valve replacement surgery is a well-established therapy that reduces symptoms and increases survival rates. However, the procedure may be associated with high operative mortality rates and promote comorbidity. Depending on the local reality, the prevalence of patients considered inoperable (due to medical comorbidities and age) may achieve 30%. For these patients, transcatheter aortic valve implantation (TAVI) was initially indicated; over time, the method has advanced technologically and been simplified, and become an alternative therapy for patients at low and intermediate surgical risk also, and considered one of the major advances of modern medicine.

Introduction

Aortic stenosis is an insidious disease with a long latency period. It has a rapid progression after the onset of symptoms, resulting in a high mortality rate (approximately 50% in the first two years) in untreated asymptomatic patients,[1-3] in whom sudden death is common. Duration of asymptomatic stage is variable. The prevalence of aortic stenosis is increasing due to population aging and is considered the most common valve disease requiring intervention.[4]

Valve replacement surgery for treatment of aortic stenosis reduces symptoms and increases survival rates.[5-7] In general, surgical mortality is 1-3% in individuals younger than 70 years and 408% in the elderly. Despite the higher risk, age alone cannot be considered an absolute contraindication, since favorable outcomes have been reported even in patients aged 80 or older.[8-10]

In clinical practice, surgical treatment is not indicated for nearly 30% of patients (this can vary from one region to another) due to high-risk medical conditions.[11-14] Some of these include advanced age, female sex, functional class, surgical emergency, ventricular dysfunction, pulmonary hypertension, previous cardiac surgery, and coronary artery disease. In these cases, a less invasive procedure – transcatheter aortic valve implantation (TAVI) – may be indicated.

TAVI was first performed in 2002 by Professor Alain Cribier, who showed that it was possible to repair severe aortic stenosis by TAVI in a critically-ill patient.[15] With global dissemination and accumulated experience, technological advances in TAVI have been made; the technique has been simplified and become a low-risk therapeutic option for patients at intermediate surgical risk. In the last 15 years, more than 350,000 procedures have been performed in approximately 70 countries.[16] medicine.

Indications

Based on recent studies, indications for TAVI now encompass all risk groups. Clinical benefits of TAVI was initially shown in patients with severe calcific aortic stenosis, advanced age and high surgical risk (The Society of Thoracic Surgeons, STS > 10%, Euroscore > 4%). The most relevant studies have shown that TAVI is not inferior to heart valve replacement surgery in terms of one-year follow-up mortality in high-risk patients. In addition, compared to standard therapy, it would be necessary to treat five patients to prevent one death in one-year period.[17,18]

Keywords

Aortic Valve Stenosis; Percutaneous Aortic Valve Replacement; Aged; Risk Factors; Morbidity; Mortality.

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TAVI has also become a therapeutic option to treat patients with STS-defined intermediate risk since publication of the PARTNER2[19] and SURTAVI[20] clinical trials.

In 2020, with publication of the PARTNER3[21] and EVOLUT LOW RISK[22] clinical trials, TAVI has been recognized as one the main revolutionary therapies of contemporary medicine and become indicated for low-risk patients also (STS<4%). The PARTNER3 study, conducted in 71 centers with patients with mean age of 73 years and STS 1.9%, showed the superiority of TAVI for the primary composite endpoint (death, stroke and rehospitalization) in one-year follow-up. The secondary endpoints showed a lower incidence of new atrial fibrillation within 30 days, lower hospitalization rates and more effective control of heart failure-related symptoms (according to the KCCQ score and the 6-minute walk test). The EVOLUT LOW RISK,[22] conducted on patients at same age range, analyzed the composite endpoint of death and stroke in 24-month follow-up. The study showed lower incidence of debilitating stroke, acute renal failure, bleeding-related complications, and atrial fibrillation. On the other hand, the study showed higher incidence of moderate-to-severe aortic regurgitation and need for pacemaker implantation.

A study conducted by the FDA with 30 days of follow-up showed zero mortality in low-risk patients treated with TAVI, as well as a shorter length of hospital stay and lower incidence of atrial fibrillation, corroborating the safety of the therapy.[23] Clinical and echocardiographic results have been recently published in the five-year follow-up NOTION clinical trial. Despite its limitations, including the small number of participants, the study brings relevant results of a longer follow-up. The study concluded that there were no significant differences between the patients undergoing TAVR and patients undergoing surgical aortic valve replacement in all-cause mortality, stroke, or myocardial infarction.[24]

Calcification of tricuspid prosthetic valve is considered the most common cause of aortic stenosis, as shown in Figure 1. This entity is no longer considered "degenerative" because of its complex and highly regulated pathophysiological basis, marked by an active and highly regulated process. It involves mechanisms that may occur simultaneously and contribute to disease development, including chronic inflammation, lipoprotein deposition, activation of the renin-angiotensin system, osteoblastic transformation of valvular interstitial cells and active calcification.[25-28]

The incidence of bicuspid aortic valve stenosis is higher in young than in older subjects. Individuals older than 80 years account for approximately 20% of surgeries.[29] Some anatomical features of this condition, such as the oval-shaped annulus, and uneven calcification and size of the leaflets, may lead to less predictable outcomes of the TAVI. However, a recent meta-analysis with 13 observational studies including data of 758 patients with bicuspid valves showed a successful rate of 95% of the procedure.[30,31] Early events rates, including all-cause mortality, stroke, life-threatening bleeding, vascular complications and valve dysfunction, were not different between patients with bicuspid and tricuspid valves. Also, no difference was found in the rate of annular rupture between the groups. However, a higher need for pacemaker implantation was observed and the combined incidence of moderate-to-severe paravalvular regurgitation was 12.2%.[30]

Valve-in-valve (ViV) TAVI has emerged as a novel, less invasive approach for bioprosthetic aortic valve degeneration treatment. The use of the MEDTRONIC (CoreValve, Evolute R and Evolut Pro) and EDWARDS (SAPIEN XT and SAPIEN 3) valves have been approved for high-risk patients. Recently, results of the PARTNER 2 ViV registry[33] of a study on the safety and effectiveness of self-expanding TAVI[34] have been published. The first study reported 30-day and one-year mortality rates at one year of 2.7% and 12.4%, respectively, and in the second, these rates were of 2.2% and 14.6%, respectively. Moderate or severe aortic regurgitation occurred in 3.5% of the patients. Factors significantly associated with higher residual aortic gradients were surgical valve size, stenosis as modality of surgical valve failure, and presence of surgical valve prosthesis-patient mismatch.[33,34]

A recent review of five meta-analyses[35-39] comparing ViV TAVI to the new surgical procedure showed similar mortality rates (in-hospital, 30-day and one-year mortality) between the groups, even considering that patients that underwent ViV TAVI were at higher surgical risk. Thirty-day mortality of ViV TAVI reported in these meta-analyses was not different than that reported in the VIVID registry,[40] with a non-significant tendency toward a higher rate in the VIVI-registry (7.6% vs. 4.4%, p>0.05).

The experience has shown that complications of ViV TAVI can be prevented. Patients with small surgical bioprostheses represent a particular challenge, as they seem to show higher residual gradient and higher late mortality than patients undergoing ViV TAVI.

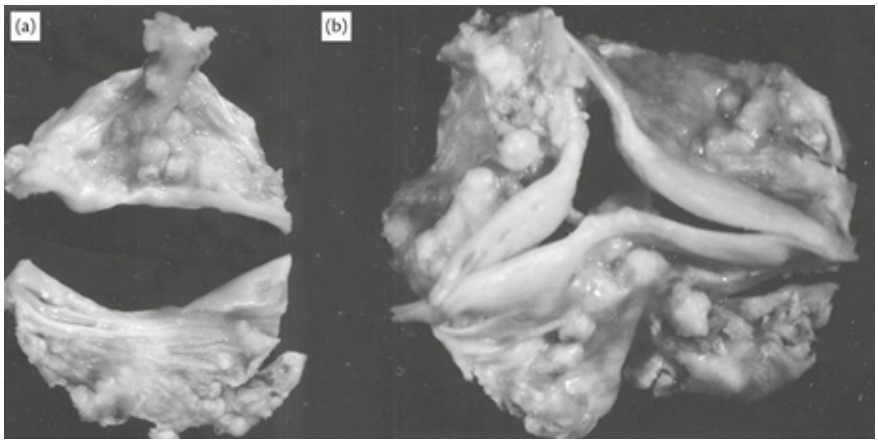

Figure 2 – Calcified bicuspid (A) and tricspid (B)aortic valve[32]

Supra-annular bioprosthetic valves and a high implant could mitigate this complication.[41] More recently, some researches have described a technique involving bioprosthetic valve fracture with a high-pressure balloon to facilitate ViV TAVI. The strategy seemed to facilitate the expansion of the transcatheter valve, with reduction of residual transvalvular pressure gradients.[42]

Clinical Indication

According to recent guidelines, TAVI is indicated for symptomatic patients with an average gradient greater than or equal to 4m/s. For patients with low gradient and low flow, valve area smaller than or equal to 1cm^2, and reduced ejection fraction, the indication continues for those with preserved flow reserve (which can be analyzed by dobutamine stress echocardiogram). For patients with preserved ejection fraction and no flow reserve, the severity of stenosis can be estimated by calculation of calcium score by computed tomography.[43]

Immediate and Late Results

After successful valve replacement surgery, the symptoms and quality of life generally improve, although with a longer recovery time as compared with TAVI. Operatory mortality rates vary from 1 to 8%, and long-term survival is comparable to that in the general elderly population of same age.[8-10] Younger subjects have shown substantial improvement with valve replacement surgery compared with conservative medical therapy, with low survival rates though. Risk factors for late mortality include age, comorbidities, severe symptoms, left ventricular dysfunction, ventricular arrythmias and untreated coronary artery disease.[44,45]

For those cases with well-defined indications, TAVI has been shown as a feasible procedure. Constant improvement in early mortality and complication rates has been shown with accumulated experience, improved pre-procedural image processing and better techniques regarding respective valves and delivery systems. While 30-day mortality rates varied from 5% to 15% in the first reports,[17,46-48] more recent studies using late-degeneration devices have shown a decrease by 1-2% in these rates, varying from 5% to 7%.[49,50]

With respect to long term survival, studies have reported a one-year survival rate of 60-85% in patients at high risk, greatly depending on the severity of comorbidities,[17,18,46,48,51-53] reaching 95% in patients at intermediate risk. Although improvement of health and quality of life at one year after TAVI is comparable to that seen in open surgeries, it emerges faster in case of TAVI, due to its less invasive nature.[45,52] Long-term durability of these procedures has been carefully studied, although no difference has been reported in five-year outcomes between transcatheter and surgical bioprosthetic aortic valves.[54,55]

Table 1 summarizes the main outcomes of TAVI of clinical trials. Overall and individual analyses showed that vascular complication rates, need for pacemaker implantation, and paravalvular regurgitation rates were higher in TAVI than conventional open surgery.[20,56] On the other hand, severe bleeding, acute renal injury and new-onset atrial fibrillation were significantly more frequent in open surgery than TAVI, and no statistically significant difference was seen in cerebrovascular event rates.[19,56]

Table 1 – Outcomes of transcatheter aortic-valve implantation obtained from clinical trials

	Partner A	Partner B	Partner 2	Core Valve	SURTAVI	Partner 3	ELR*
N	348	179	1011	394	879	1000	1403
Age	83.6	83.1	81.5	83.2	79.9	73.3	74
Female (%)	42.2	54.2	45.8	46.4	42.2	32.5	36
STS risk-score (%)	11.8	11.6	5.8 +- 2.1	7.3 +- 3	4.4 +- 1.5	1.9	1.9
Prosthesis	SAPIENTM	SAPIENTM	SAPIENTM XT	Core Valve TM	Core Valve TM (16% Evolut R TM)	SAPIENTM3	Core ValveTM Evolut RTM . Evolut PROTM
30-day mortality (%)	3.4	5	3.9	3.3	2.2	0.4	0.5
30-day stroke (%)	3.8	6.7	5.5	4.9	3.4	0.6	2.1
Moderate-to-severe regurgitation (%)	13.1	15	3.7	10	5.3	0.6	4.3
Pacemaker (%)	4.4	3.4	8.5	19.8	25.9	7.3	19.4
Vascular event (%)	11	16.2	7.9	5.9	6	2.8	3.8
Major bleeding (%)	9.3	16.8	10.4	28.1	12.2	7.7	3.2
Acute renal injury (%)	2.9	1.1	1.3	6	1.7	0.4	0.9
New-onset AF (%)	8.6	0.6	9.1	11.7	12.9	7.0	9.8
One-year mortality (%)	24.3	30.7	12.3	14.2	6.7	1.1	2.4
Two-year mortality (%)	33.9	43.3	16.7	22.2	11.4		
Five-year mortality (%)	67.8	61.8	-	-			

**ELR=Evolut Low Risk Trial; STS: Society of Thoracic Surgery; AF: atrial fibrillation*

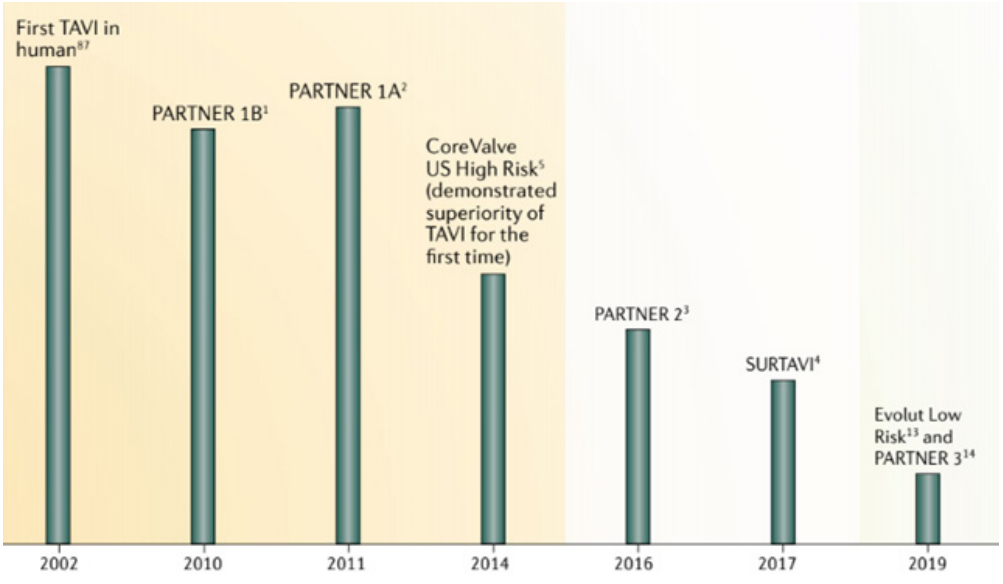

Figure 3 – Chronological sequence of published clinical trials[57]

The decision towards a therapy is made based on clinical, anatomical, and technical aspects that may be considered alone or in combination. Some conditions, such as previous cardiac surgeries, restricted mobility, frailty, chest irradiation sequelae, porcelain aorta, chest deformity, marked scoliosis, and obesity favor the choice of TAVI. On the other hand, open surgery is the preferred procedures in case of unfavorable access for TAVI, suspected endocarditis, short distance between coronary ostia and annulus, ascending aorta aneurysm, aortic or left ventricular thrombus, other valvular dysfunction, coronary artery disease and need for bypass revascularization, and septal hypertrophy.

Procedure

In the periprocedural period, some aspects should be considered without compromising patient's safety. The procedure may be performed in a cath lab instead of a hybrid room. If performed via a transfemoral approach, the presence of a cardiac surgeon is not obligatory, but the professional should be involved in the process and be available in case of complications. The staff should include at least two surgeons, one nurse and one X-ray technician. The presence of an echocardiographist, anaesthesiologist, cardiac surgeon, vascular surgeon and perfusionist in the catheterization laboratory is not an absolute requirement, but they should be involved in selected and more complex cases or in those at the initial phase of the learning curve.[58]

The first implants were conducted via an antegrade transseptal approach. Over the years, this approach has been abandoned in favor of the transfemoral approach, which is the method of choice, in addition to alternative routes (transapical, trans-aortic, trans-subclavian, transcarotid). An accurate analysis, guided by computed tomography coronary angiography, is essential for the selection of the access route, considering vessel anatomy, the profile and size of the device.[59]

Immediately after the procedure, all patients should be monitored in the hybrid operating room for at least 10-15 minutes, with special attention to hemodynamics and cardiac rhythm. Then, the patients should be transferred to a coronary care unit or to a cardiac telemetry unit, according to local protocols. Patients' clinical status, especially concerning the procedural outcomes, echocardiogram, and laboratory results, should be carefully evaluated. Mobilization should be prescribed a few hour later, in the absence of vascular access problems (e.g. hematoma or bleeding) and removal of temporary pacemaker. Patients without complications (or those whose complications were successfully managed) can be discharged on the next day.[58]

The efforts to accelerate recovery and mobilization require shorter hospitalization time and minimize unnecessary use of resources. Hospital discharge within 24-72 hours after the procedure seemed not to affect the safety of the procedure, as reported in previous studies.[60-62] A clinical protocol of early discharge tested at low-, medium-, and high-volume TAVI centers showed excellent safety and efficacy outcomes.[63] The most common problems involved in a prolonged hospitalization include conduction disturbances, bleeding and acute renal injury. Monitoring of atrioventricular block is by far the most important measure.

The cost-benefit relationship of the minimalist approach in TAVI has not been well defined. In a small U.S. series of 142 patients (n=70 undergoing minimalistic transfemoral TAVI and n=72 undergoing standard transfemoral TAVI), it was demonstrated that that the minimalistic strategy decreased the cost of TAVI (USD 2,869 estimate) and could be used frequently to prevent costs associated with hybrid operating rooms and anesthesia.[64]

Although TAVI is a complex procedure, important advances toward its simplification have been made. In many centers, the minimalist approach has been routinely performed and shown to be as safe and effective as the standard approach.

Complications

Despite technical advances in the development of implantation techniques and devices, in addition to more possible procedures and indications, potential complications may occur and do require consideration and prevention. The first complications of TAVI were peri and post-procedural neurological, conduction disturbances, and events vascular complications, peri neurological events, and perivalvular regurgitation.[15,16] More recently, despite their low incidence, increasing interest has been devoted to aortic rupture and coronary occlusion due to their potential and severe impact.[34,65] However, other concerns have concomitantly emerged regarding durability and risk of thrombosis, since procedures have been performed in younger and at lower-risk patients.[66-68]

Therefore, the fact that TAVI is indicated for younger patients today make mandatory the recognition and

monitoring of possible complications related to durability of the procedure, since these patients have higher life expectancy, and calcium metabolism that accelerates leaf calcification compared with those patients for whom TAVI was first indicated. Failure of the procedure may be related to deterioration (consequent to calcification, pannus or thrombus formation) or intraprosthetic regurgitation (e.g. reduced leaflet mobility and endocarditis).[69]

No significant increase in average gradient or structural valve deterioration was reported in the five-year follow-up in the PARTNER study. Results of follow-up of up to five years have also been described in other three studies,[70-72] two of them did not raise important issues regarding durability, with stable transprosthetic pressure gradient over time and dysfunction rates of 3.4% and 4.2%, respectively, based on different definitions.

With respect to late durability, some studies have presented data from 7-8 year-follow-up using a SAPIEN (Edwards Lifesciences) or a CoreValve device. Three different studies conducted in one center reported stable transprosthetic gradient over time, and severe prosthetic dysfunction rates of 2.4%, 3.2% and 3,6%.[73-75] Holy et al.,[76] evaluated long-term results of 152 consecutive patients undergoing TAVI with the self-expanding CoreValve between 2001 and 2011.[76] Echocardiographic follow-up at 6.3±1.0 years (5.0-8.9 years) was 88% complete (60 out of 68 survivors beyond five years). No evidence of structural valve deterioration was reported, and five patients (3.3%) had undergone redo TAVI or surgery due to paravalvular leakage. Deutsch et al. reported an overall crude cumulative incidence of structural valve deterioration of 14.9% (CoreValve 11.8% vs. SAPIEN 22.6%; p=0.01) at seven years.[77]

Vascular complications such as bleeding, need for transfusion and hemodynamic instability were initially identified as major limitations of TAVI. However, with improvement of the devices and in patient selection, and accumulated experience, these complications have become rarer. Today, the mean complications are minor bleeding and direct damage such as dissection and occlusion of the vessel.[78]

Cerebrovascular events are associated with high morbidity and mortality. A meta-analysis of 64 studies involving 72,318 patients found an incidence of cerebrovascular events of 3.3% within 30 days post-TAVI.[79] Nearly half of the events occurred 24 hours following the procedure and the others attributed to catheter manipulation via aortic valve, balloon dilatation and prosthesis release. Neurological events clinically manifest as focal signs or even silent ischemia, detected by brain magnetic resonance imaging.[16,80] More recent studies have reported a favorable trend of decrease in the incidence of events to nearly 1.2% at one year, particularly with improvement of devices and growing experience.[21] In addition, protective devices have been developed to filter or deflect debris from cerebral vasculature.

The most common conduction disturbances are left bundle branch block and total atrioventricular block.[81] Efforts have been made to prevent these complications, as they are associated with lower recovery of left ventricular function, greater need for pacemaker and rehospitalizations, and longer hospital stay. The assessment of valvular anatomy and selection of the most appropriate prosthesis not always minimize these effects.

Paravalvular leak may occur and has been more commonly associated with TAVI and standard surgery.[16,82] The incidence of moderate-to-severe leakage in first generation devices were reported in 12-21% of the cases.[82] This deserves special attention and prevention, due to its relationship with high morbidity and mortality.[83] The three mechanisms involved are incomplete apposition of TAVI to the valve annulus because of severe calcification, undersizing and poor positioning of the prosthesis. In more recent series, the incidence of leakage significantly decreased, as mentioned previously. This is explained by a more precise evaluation of the valve annulus before surgery, by computed tomography angiography, ability to recapture, reposition and finely adjust the valve. Other improvements include sealing skirts or an additional external sealing layer to fill the gaps between the transcatheter prosthesis and the aortic annulus.[84]

Thrombosis of bioprostheses can occur by two different mechanisms: first, as symptomatic, obstructive valve thrombosis, with increased transvalvular gradient and reduced effectiveness of the orifice measured by echocardiography. This is a rare event, reported in approximately 0.5% of the patients undergoing TAVI.[85,86] Second, as asymptomatic, subclinical valve thrombosis, with thickening and reduced motion of prosthetic valve leaflets detected by computed tomography, with normal transvalvular gradients at transthoracic echocardiography. This has been more commonly reported patients treated via a percutaneous approach., with an incidence varying form 5% to 40% in patients with TAVI.[86] The RESOLVE and SAVORY,[68] an observational study on subclinical leaflet thrombosis has reported an incidence of 4% of

Table 2 – Composite endpoints defined by the VARC2[88]

Device success
Absence of periprocedural mortality AND
Correct anatomical positioning AND
Intended performance of the prosthesis (no prosthesis-patient mismatch and mean aortic valve gradient<20 mm Hg or peak velocity<3 m/s, and no moderate-to-severe aortic valve regurgitation)
Early safety
All-cause mortality
Stroke
Major bleeding
Acute kidney injury
Coronary artery obstruction requiring intervention
Major vascular complication
Valve-related dysfunction requiring repeat procedure (BAV, TAVI, SAVR)
Clinical efficacy
All-cause mortality
Stroke
Requiring hospitalizations for valve dysfunction or heart failure-related symptoms
NYHA class III or IV
Valve dysfunction (mean aortic valve gradient ≥ 20 mm Hg, EOA ≤ 0.9–1.1 cm2 and/or DVI<0. 35 m/s, and/or moderate-to-severe valve regurgitation)
Long-term safety
Structural valve deterioration
Valve dysfunction (mean aortic valve gradient ≥20 mm Hg, EOA ≤0.9-1.1 cm2 and/or DVI<0.35 m/s, and/or moderate-to-severe valve regurgitation
Requiring repeat procedure (TAVI or SAVR)
Prosthetic valve endocarditis
Prosthetic valve thrombosis
Thromboembolic events (e.g., stroke)
Bleeding, unless clearly unrelated to valve therapy (eg, trauma)

BAV: Balloon aortic valvuloplasty; TAVI: transcatheter aortic valve implantation; SAVR: surgical aortic valve replacement

this event in 138 patients undergoing standard surgery and 13% in 752 patients undergoing TAVI. Subclinical leaflet thrombosis was also less frequent in patients receiving anticoagulants, compared with those in double antiplatelet therapy (4% vs. 15%; p< 0.0001).[68] An incomplete frame expansion of TAVI, as well its metallic nature seem to be two of the main risk factors for subclinical thrombosis.[84]

Endocarditis, although less common after valve replacement surgery (0.5-3.1%;[58] 1-6%[84,87]), can be a severe complication. In a recent multicenter registry, including 250 post-TAVI patients, in-hospital mortality was 36% and two-year mortality 66.7%. [61] Younger age, male sex, family history of diabetes mellitus, and moderate-to-severe residual aortic regurgitation were significantly associated with increased risk of infectious endocarditis.[61] The most common causative agents of prosthetic valve endocarditis were Staphylococci (31.5%), Enterococcus (20%) and Streptococcus (14%).[87]

Although the possibility of late failure of transcatheter aortic valve replacement is regarded as a major concern, preliminary observations revealed that, in contrast to reoperation following the conventional surgical procedure, which is technically challenging with a significant risk of morbidity and mortality, the redo TAVI seems to be safe and effective.[62]

In summary, understanding the complications is extremely important for the planning of the procedure. The association of these complications with patients' profile has become more and more important, since, as evidence has shown, indication of TAVI has been expanded for younger and at lower-risk patients.

With the aim of defining endpoints that reflect clinical efficacy of the device and patients' safety, the Valve Academic Research Consortium (VARC) consensus was created in 2011. One year later,

the document was updated, with the objective to broaden the understanding of risk stratification of the patient and selection of the cases, and to revise the endpoints for the development of clinical trials. Thus, the so-called VARC-2 recommends the inclusion of a time-related valve safety, which combines valve dysfunction, endocarditis, and thrombotic complications. Table 2 describes the composite endpoints defined in this document.[88]

Antithrombotic Therapy

Current guidelines are based mainly on specialists' opinions and recommend double antiplatelet therapy in the first six months, followed by low dose aspiring throughout life. For patients with atrial fibrillation (AF), the use of vitamin k antagonists is recommended.[89,90]

AF is a predictor of stroke and systemic embolism and can be found in up to one third of patients with indications for TAVI. Due to the need for anticoagulation, patients undergoing TAVI are at increased risk for hemorrhagic events after the procedure and during follow-up.[91] In case of hemorrhagic complications in patients with concomitant AF, mortality at one year after TAVI increases to 50%.[92] Therefore, evaluation of the ideal antithrombotic therapy in this population should be carefully considered.

The use of novel oral anticoagulants (NOACs) in patients undergoing TAVI, without formal indication for anticoagulant therapy is still under investigation. In the recent GALILEO study,[93] the use of rivaroxaban at a dose of 10 mg daily (combined with aspirin at a dose of 75 to 100 mg) was tested in 1,644 after successful TAVI. A higher incidence of death, thromboembolic complications and life-threatening bleeding was observed in the rivaroxaban group compared with the antiplatelet group. Additional studies evaluating the effects of other NOAC are ongoing, including the ATLANTIS and the ENVISAGE-TAVI AF, and their results are expected to be published soon.

Guidelines

According to the American Heart Association (AHA), American College of Cardiology (ACC) and Society of Thoracic Surgery (STS), indications for TAVI have changed to high-risk patients (class I; level of evidence A) and as alternative therapy for patients at intermediate risk (class IIa; level of evidence B).[94] European guidelines have followed the same trend, corroborating the indication for patients at intermediate or high surgical risk (STS score or EuroSCORE > 4%) and mainly for elderly, inoperable patients (class I; level of evidence B).[43]

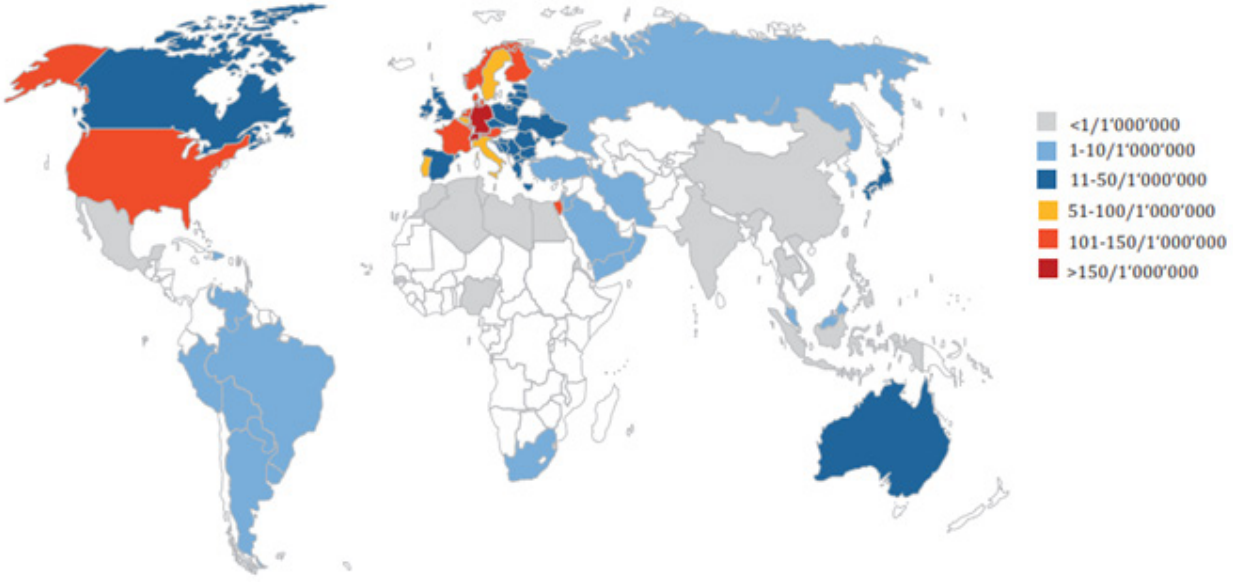

Figure 6 – Geographic dispersion of transcatheter aortic-valve implantation in the world. The legend indicates the number of procedures per 1,000,000 inhabitants.[95]

Future Perspectives

Today, the greatest challenges are related to TAVI durability, and several limitations prevent a more robust evaluation. First, TAVI is a relatively young technology, since its use started to expand only after the procedure received the CE mark in 2007 and was approved by the US Food and Drug Administration in 2011. This means that there may be few data available on valve durability during periods longer than 10 years. Second, currently available data from five-year follow-up studies a related to first generation devices, implanted by relative inexperienced operators, with higher rates of improper positioning of the valve and size-related problems. Finally, the main limitation of durability over time is older age of patients, multiple comorbidities and the high risk due to lower life expectancy, and consequently a small number of patients (generally less than 50% of initial population) in the long-term follow-up.

Another important issue is the optimization of antithrombotic therapy after device implantation. As previously mentioned, ongoing studies are expected to be published soon, and can modify or not currently established practices.

Aortic Regurgitation

Data are still limited for analysis of safety and efficacy of TAVI in patients with pure aortic regurgitation. Its application, even in those at high surgical risk is off-label. Most devices that have been approved worldwide are for the treatment of aortic stenosis.

The prevalence of aortic regurgitation increases with age and affects nearly 13% of patients with native left-sided valvular heart disease. The symptoms tended to disappear late in the course of the disease with the onset of left ventricular dilatation and systolic dysfunction. Patients with ejection fraction lower than 30% have an annual mortality risk of 20%.[96]

Based on current European and North American guidelines, a surgical procedure should be considered for patients with moderate or severe symptomatic aortic regurgitation, and reduced left ventricular systolic function (<50%) or severe left ventricular dilatation (left ventricular end-systolic diameter > 50mm, left ventricular end-diastolic diameter > 65-70mm; or left ventricular end-systolic volume >45mL/m^2).[97,98] However, there is a high-risk subgroup of inoperable patients for whom TAVI should be considered.

The main challenge for TAVI procedure is the absence of annular and leaflet calcification, which is required for anchoring and stabilization of the device during its implantation. The lack of calcium, secondary increased systolic volume, and dilation of the aortic root are limitations for proper positioning of the prosthesis and predispose to moderate or severe embolization or regurgitation after the procedure (which are associated with worse clinical outcomes).[99] Migration of the valve may occur in the aorta or deeper in the left ventricle up to several hours post-implantation. Over-dimensioning of the valve has been proposed to reduce the risk of migration – an oversizing of 15-20% has been recommended - no greater than that, to avoid the risk of annular rupture and abnormalities in the conduction system.[100,101]

New generation devices, such as the CoreValve, Evolut R, ACURATE neo, Lotus and Sapien 3, have some resources that make them different from previous devices. Characteristics like ability of retrieval and repositioning in the case of self-expansible, and adaptative sealing skirt of the Sapien 3 and Lotus, enable a more controlled and predictable TAVI.[102,103] The authors reported the safety and early clinical efficacy of TAVI in 254 patients from 46 centers. The authors reported the device success, defined according to the VARC-2 criteria, of 67%.[104] Yoon et al.,[105] studied 331 patients from 40 centers, and reported a device success of 74.3%.[105]

Author Contributions

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Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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This study is not associated with any thesis or dissertation work.

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