Since its introduction, transcatheter aortic valve replacement (TAVR) has evolved rapidly from an experimental to a routine intervention. Randomized trials clearly demonstrated that TAVR offers a survival benefit in inoperable patients and has early mortality and midterm survival outcomes equal to those of standard surgical aortic valve replacement (SAVR) in a high-risk population. These excellent results have led to guideline recommendations in the United States and Europe promoting the use of TAVR in populations of inoperable and high-risk patients provided that the decision is based on a heart team discussion. With improvements in valve design, the development of smaller delivery systems, and the introduction of improved mechanisms for steering, stable positioning, and recapturing, the use of TAVR has expanded continuously. Nationwide registries have contributed to large data sets confirming acceptable results outside clinical trials. Parallel to the publication of registry data and large center series, a plethora of case reports have documented the growing off-label use of TAVR for the treatment of degenerated bioprostheses (valve-in-valve implantation) and aortic insufficiency and in lower-risk patient subsets who until now have not been addressed by randomized trials. As TAVR has become a standardized procedure, many operators have become proficient in performing it, and patient recruitment has become more challenging, particularly in high-volume centers. The natural evolution seems to be an expansion of the indication for TAVR to lower-risk patients.

The European guidelines on valvular heart disease clearly state that “at the present stage, TAVR should not be performed in patients at intermediate risk for surgery and trials are required in this population.” Despite the absence of sufficient data to support TAVR in low-risk patients, aggressive direct patient marketing, self-referral bias, and ignorance of the heart team concept have slowly led to an erosion of these guideline recommendations. In some countries, TAVR is already routinely applied in lower-risk and younger patient groups (Figure 1).

The use of TAVR shows a large variation across nations in Europe. The number of TAVR implants per million ranged in 2011 from 6.1 in Portugal to 88.7 in Germany. Germany (36.2%) and Switzerland (34.5%) had the highest and Portugal (3.4%) and Spain (8.4%) had the lowest penetration rates. The observed correlation between TAVR use and healthcare spending per capita \((r=0.80, P=0.005)\) indicates that reimbursement rather than medical indication is a major driver for the expanded use of TAVR. Not surprisingly, TAVR-specific reimbursement systems were associated with higher TAVR use than restricted systems (698±232 versus 213±112 implants per 1 million individuals ≥75 years of age; \(P=0.002)\). A percutaneous therapy, particularly when delivered under local anesthesia, will be preferred by patients over a surgical procedure involving cardiopulmonary bypass and some sort of a thoracotomy or sternotomy, even if the risk-benefit ratio and long-term outcomes are largely unknown. If patients are advised to or choose to undergo TAVR outside the current guideline indications, they should be made aware of the following.

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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This article is Part II of a 2-part article. Part I appears on p 2321.

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Response by Haussig and Linke on p 2342
About SA VR
SAVR is a procedure with a history of >50 years of continuous improvements. It is safe and can be performed through a limited thoracotomy or ministernotomy with excellent outcomes and proven long-term durability. Morbidity and mortality rates are low, and hemodynamic performance is good. Additional procedures, including root replacement, aortic surgery, left ventricular outflow tract resection, other valve surgery, or revascularization, can be performed at the same time.

In a review of some 108,687 patients who had an isolated SA VR and were included in the Society of Thoracic Surgeons database from 1997 to 2006, the overall mortality and risk-adjusted mortality decreased by 24% and 33%, respectively. Mortality was 0.6% in patients <60 years old, <1.3% in patients <70 years old, <3.5% in patients <80 years old, and <5% in patients <85 years old.11 These data have been confirmed by numerous national databases. In a recent meta-analysis including 48 studies of SA VR in octogenarians, the rates for mortality were 6.7% (in the period from 2000–2006, 5.8%); stroke, 2.4%; dialysis, 2.6%; and pacemaker implantation, 4.6%. Survival was 88% at 1 year, 79% at 3 years, 65% at 5 years, and 30% at 10 years of follow-up.12 In a contemporary study of high-risk patients (mean age, 80.4±3.6 years; mean logistic EuroSCORE, 13%±7%), the hospital mortality after SAVR was 1.3%.13 Quality of life is good after SAVR, and the procedure is cost-effective.

TA VR Does Not Improve Survival in Operable High-Risk Patients
A meta-analysis including 4873 patients from 17 studies (randomized, clinical trials and adjusted observational comparative studies) showed that TA VR does not reduce early (at 30 days or in hospital) or midterm (at 3 months–3 years) all-cause mortality compared with SAVR in high-risk patients with aortic stenosis.13 In another meta-analysis comparing 4659 patients with severe aortic stenosis who underwent TA VR (n=2267) and SAVR (n=2392), 30-day all-cause mortality was not significantly different between groups (relative risk [RR] 1.00; 95% confidence interval [CI], 0.8–1.23; P=0.97). The subgroup analysis of randomized, controlled trials also did not show any significant difference in 30-day all-cause mortality between the TAVR and SAVR groups (RR, 1.53; 95% CI, 0.99–2.36; P=0.06). Midterm all-cause mortality was also not significantly different between the TAVR and SAVR groups (RR, 0.78; 95% CI, 0.59–1.02; P=0.07) at 85 weeks of mean follow-up.14

Because TA VR does not improve survival even in the group of patients considered at the highest risk for surgery, it is unlikely that it will improve survival in younger, low-risk patients. Some rare but potentially lethal complications such as coronary occlusion, annular rupture, ventricular perforation, and vascular injury are procedure related. These complications are largely independent of age and the underlying risk and can therefore be expected to contribute to the procedure-related mortality in all patient subsets.

There are in fact indications for excess mortality with TA VR in a low-risk group of patients. Results from the German Aortic Valve Registry (GARY) show no difference for mortality in high-risk stratified groups with a euroSCORE >20.15 In lower-risk groups, however, SAVR shows a significant survival benefit in both groups with a logistic euroSCORE of 10 to 20 (P<0.001) and <10 (P<0.001).15

Stroke Remains an Issue With TA VR
Using diffusion-weighted magnetic resonance imaging, new ischemic lesions can be detected in up to 90% of patients after TAVR, a rate that is significantly higher than in patients undergoing SAVR.16 The periprocedural incidence of cerebrovascular events after TAVR therefore exceeds that after any other cardiac intervention or valve surgery.17 Randomized trials in high-risk populations have consistently shown an increased stroke rate with TAVR compared with SAVR.3,18,19 A pooled meta-analysis of these randomized, clinical trials also demonstrated a significantly higher
incidence of stroke with TAVR compared with SAVR (RR, 0.56; 95% CI, 0.36–0.88; P=0.01) at a mean follow-up of 99 weeks.13 Despite some recent reports that have shown a reduction in stroke rate associated with TAVR,6 the French Aortic National CoreValve and Edwards (FRANCE) II and Australian registries consistently demonstrate a 30-day stroke rate of 3.4% and 3.9% in the current era.5,20 It is worth mentioning that periprocedural stroke has a dismal prognosis with an up to >3.5-times increase in 30-day mortality.20,21 Passage of guide wires and large-bore catheters during valvuloplasty and device delivery, positioning, and implantation may lead to the disruption of atheromatous plaques of valvular and vascular origin during TAVR.18 Most of the events contributing to the embolic load during TAVR are related to relatively uncontrolled and remotely induced manipulation of valvular or vascular structures. Retrograde passage of the aorta and the aortic arch and dilatation and displacement of the native, calcified aortic valve may cause dislodgement of calcific debris independently of age and the underlying risk. Hemodynamic instability during or after rapid ventricular pacing can impair cerebral perfusion pressure, which may also contribute to the risk of stroke. In addition, subacute embolization may be caused by persistent lesions on the displaced (not resected) native valve leaflets. A “dead” space between the implanted prosthesis and the native leaflets or between the leaflets and the aortic wall may be prone to thrombus formation. As in SAVR, new onset of atrial fibrillation occurs frequently after TAVR and poses an additional stroke risk in the postprocedural phase. More recently, a number of embolic protection devices have been introduced to reduce the risk of stroke during TAVR. Although these devices may effectively capture some debris, so far, none of them has been proven to effectively reduce the risk of stroke. Given the low risk of stroke in all-comers after isolated SAVR (0.7% in patients <70 years of age, <2.0% in patients 70 to 80 years of age, and <2.5% in the octogenarian population),11 the question of risk versus benefit must be raised before the indication of TAVR is expanded to younger, low-risk populations.

TAVR Leaks
Paravalvular aortic leakage (PV) after SAVR is an infrequent event and occurs in <1% of patients.72 This was also confirmed in the surgical arm of the Placement of Aortic Transcatheter Valve Trial (PARTNER), with an incidence of PVL after SAVR of 0.9% after 2 years.1 On the contrary, PVL is a frequent complication after TAVR. The GARY registry reported the outcomes of 2763 patients undergoing transfemoral TAVR in 2011; 55.5% of patients had grade I and 7.0% grade II or higher aortic insufficiency as a result of PVL.6 Similar numbers have been reported from the PARTNER trial (7.0% at 1 year and 6.9% at 2 years).1 TAVR patients had significantly more total aortic regurgitation at every postimplantation time than patients in the SAVR cohort. Milder, moderate, or severe paravalvular aortic regurgitation was more common in the TAVR group at every follow-up time (P<0.0001).

In a meta-analysis, the incidence of postoperative moderate or severe aortic regurgitation, which included both paravalvular and transvalvular regurgitation, was significantly higher after TAVR than SAVR (7.8% versus 0.6%; RR, 6.82; 95% CI, 3.57–13.04; P<0.00001).21 After TAVR, patients with mild or moderate paravalvular aortic regurgitation have larger postimplantation left ventricular end diastolic dimension (P=0.009), left ventricular diastolic volume (P=0.003), left ventricular mass (P=0.001), and left ventricular mass index (P=0.007), indicating the absence of reverse remodeling in the presence of PVL. Of all echocardiographic parameters after valve implantation, mild or moderate paravalvular aortic regurgitation was the strongest predictor of death (hazard ratio [HR], 2.11; 95% CI, 1.43–3.10; P=0.0002).24 In the Italian (CoreValve) registry, postprocedural paravalvular leak of >2+ was an independent predictor of mortality beyond 30 days and up to 1 year of follow-up (HR, 3.79).7 In another report, 15% of patients with a CoreValve had moderate or severe paravalvular AR, which again was an independent predictor of 1-year mortality.25 In the GARY registry, the mortality of patients with severe aortic insufficiency was 37.5% at 30 days and 50.0% at 1 year.4 In the FRANCE II registry including 3195 consecutive patients, aortic regurgitation of grade 2 or higher was observed in 15.8% of patients undergoing TAVR and was found to be a strong independent predictor of 1-year mortality for both balloon-expandable (HR,=2.50; P=0.0001) and self-expandable (HR, 2.11; P=0.0001) valves.25 Patients with a nontransfemoral approach had a much lower risk of postprocedural aortic regurgitation than those treated through a femoral approach. This benefit was observed both for balloon-expandable (RR reduction, 30%) and for self-expanding (RR reduction, 55%) devices and was confirmed by multivariable analysis.26 An interesting finding of the FRANCE II registry was that the use of a self-expanding valve was an independent predictor of postprocedural aortic regurgitation (self-expanding valve, 21.5%; balloon expandable valve, 13.0%). These data are in line with findings from other studies.6 The difference was more striking for the transfemoral approach (21.9% versus 13.9%) than for the nonfemoral approach (10.7% versus 8%). The authors suggest that, with a transfemoral approach, control of the catheter and implantation depth is more difficult with an increased risk of PVL.26 In TAVR, the presence of bulky native aortic valve calcifications leading to incomplete prosthesis apposition, annular eccentricity, inappropriate size selection (undersizing), and problems with positioning (high or low malpositioning) has been identified as an independent predictor of PVL in patients undergoing TAVR23,26,28,29 (Figure 2). Appropriate sizing with multidetector computed tomography and template-based planning may help to may prevent inappropriate valve selection.26,30 New-generation devices with supra-annular, infra-annular, or intra-annular cuffs for sealing and delivery systems that allow better control of device deployment, easy repositioning, or even removal of the device may also reduce PVL in the future. Eccentric annuli, bulky calcifications,
bicuspid anatomy, variations in annular compliance, and deformation of stents (Figure 3), all of which are associated with PVL, will, however, pose a continuous challenge for TAVR and are independent of age and the underlying risk.

Moderate or severe paravalvular regurgitation after AVR cannot be regarded a benign disease and is therefore unacceptable in a younger, low-risk population.

**Pacing Is a Risk**

Left bundle-branch block (LBBB) frequently occurs after TAVR. LBBB results in intraventricular asynchrony and may have a causative role in the development of cardiac remodeling and heart failure. The high incidence of atrioventricular block and LBBB after TAVR, especially after the implantation of self-expanding valves, has led to a remarkable need for pacemaker implantation after TAVR. The deleterious effect of new-onset, persistent LBBB on left ventricular function after TAVR has been shown in a number of studies. Patients with persistent LBBB showed either a lack of improvement or even a decrease in left ventricular ejection fraction compared with patients with no new conduction abnormalities. New onset of LBBB was reported with an incidence...
of 19.2% after TAVR with balloon-expandable devices and was persistent in 11.8% after discharge. Persistent LBBB was associated with a higher rate of pacemaker implantation, a lack of improvement in left ventricular ejection fraction, and a poorer functional status. In another series of 476 patients undergoing TAVR (including balloon-expandable and self-expanding valves), 175 (36.8%) developed new LBBB, 85.7% within 24 hours after TAVR, 12.0% before and 2.3% after hospital discharge. LBBB was persistent in 111 patients (63.4%). Implantation of the Medtronic CoreValve System more frequently led to new LBBB than implantation of the balloon-expandable Edwards SAPIEN valve (53.8% versus 21.7%) with less recovery during follow-up (39.0% versus 9.5%). In the Houthuizen et al. study, which had a much longer follow-up than previous trials (median follow-up, 915 days [578–1234 days]), persistent LBBB was also associated with a significant increase in mortality compared with the absence of LBBB and temporary LBBB combined (HR, 1.49; 95% CI, 1.10–2.03; P=0.01). In the GARY registry, the rate of new pacemaker implantation after SAVR was 4.6% as opposed to 23.6% after transfemoral TAVR. In a meta-analysis including 7 observational and 2 randomized trials, the rate of pacemaker implantation was significantly higher after TAVR than SAVR (13.2% versus 3.0%; RR, 3.53; 95% CI, 1.79–6.97; P=0.0003).

Chronic right ventricular pacing is known to be associated with left atrial remodeling, reduced atrial function, and left ventricular dyssynchrony, resulting in impaired left ventricular function, limited exercise capacity, and progressive left ventricular remodeling, finally leading to heart failure. Permanent right ventricular pacing may cause or worsen heart failure, especially in patients with impaired left ventricular function. Patients with chronic right ventricular pacing are also at higher risk for development of atrial fibrillation.

At 6 months after TAVR, patients requiring pacemaker implantation demonstrated attenuated improvement in left ventricular ejection fraction (−0.9±8.7% versus 2.3±10.8%, respectively; P=0.03) and left ventricular stroke volume (−2±16 versus 4±10 mL/m² respectively; P=0.015), a trend toward a smaller reduction in systolic pulmonary artery pressure (−1±12 versus −6±10 mmHg, respectively; P=0.09), and deterioration of the right ventricular index of myocardial performance (−3±17% versus 5±26%, respectively; P=0.05). Besides the negative hemodynamic effects of right ventricular pacing, other complications are associated with pacemaker implantation. In a population-based study including 46,299 consecutive pacemaker patients with long-term follow-up, the incidence of infection and removal of the device after first pacemaker implantation was 1.82 in 1000 pacemaker-years and after replacement procedures was 5.32 in 1000 pacemaker-years. Surgical site infection after first pacemaker implantation occurred at an incidence rate of 4.82 per 1000 pacemaker-years after first pacemaker implantation and 12.12 per 1000 pacemaker-years after replacement. Lead-related reinterventions can be expected at a rate of 2.3% after dual-chamber pacemaker procedures. Other complications such as tricuspid regurgitation and the need for subsequent device and battery changes have to be factored in.

If the indication for transcatheter aortic valve implantation is to be expanded to a younger population at less risk, a substantial number of patients will be subjected to new onset of persistent LBBB, which may impair left ventricular function, and to decades of pacing with all the associated consequences.

**Bioprosthetic Valves in Younger Patients?**

Most risk scores (euroSCORE, Society of Thoracic Surgeons) weigh age heavily. Expanding indications to lower-risk groups therefore automatically implies expanding indications to younger patients. This brings the question of valve selection (mechanical versus biological) into focus. Although for decades surgeons have promoted and expanded the use of biological valves in younger patients, recent evidence suggests an increased mortality in younger patients receiving bioprostheses.

An analysis of data from 24,410 patients with biological AVR and 14,789 patients with mechanical SAVR 65 to 80 years of age included in the Society of Thoracic Surgeons Adult Cardiac Surgery Database from 1991 to 1999 compared the long-term outcomes of patients with bioprosthetic versus mechanical AVR. In the youngest patient group (65–69 years of age), patients receiving a bioprosthesis had a substantially elevated 12-year absolute risk of reoperation (10.5%) and a 23% increased mortality rate (adjusted HR, 1.23; 95%, CI, 1.16–1.31).

This finding was confirmed by 2 propensity-matched studies in patients undergoing bioprosthetic or mechanical AVR. In a study of 206 patients ≤60 of age, biological AVR was associated with reduced midterm survival despite similar valve-related event rates in both groups.

In another study on 440 patients 50 to 70 years of age, multivariate analysis demonstrated that mechanical valves were protective for late survival (HR, 0.48; 95% CI, 0.35–0.67; P<0.01).

The freedom from structural valve deterioration of surgically implanted bioprosthesis valves is dependent of the age at implantation. At >70 years of age, a 15-year freedom from structural valve deterioration of >90% can be expected. In patients ≤60 years of age, only 63% of the valves are free of structural deterioration at 15 years. There is little reason to believe that TAVR will change this pattern. The need for crimping, balloon dilatation, stent deformation, and overexpansion or underexpansion, which may lead to unfavorable shear stress distribution of the leaflets, may cause early valve deterioration after TAVR. Most data on TAVR outcomes have been obtained in elderly, high-risk, or even inoperable patient groups with high early (10% at 30 days) and 1-year (20%–40%) mortalities and limited follow-up. The durability of the implanted valves, especially in a younger population, is therefore largely unknown.

Bleeding and thrombotic complications in patients under anticoagulant treatment have been the major drawback of
mechanical valves. A decrease in anticoagulant-related complications of mechanical valves can be expected with the more widespread use of home international normalized ratio monitoring systems that allow lower levels of anticoagulation (target international normalized ratio, 1.5–2.0) in patients with mechanical aortic valves.49

In the debate to expand the indications of TAVR to a younger population, the possible survival benefit of mechanical valves needs to be discussed with the patient.

Valve in Valve in Valve…

A frequent assumption in the TAVR age is that degenerative valve disease will be routinely treated by a single or even multiple valve-in-valve implantations in the future. This argument, which as yet is not based on any solid data, is brought forward to promote the indication for bioprosthetic valve implantation (SAVR or TAVR) in younger patients.

Several procedural adverse events and complications are more common after valve-in-valve implantation, including device malpositioning (15%), coronary obstruction (3.5%), and elevated postprocedural gradients (28% >20 mm Hg). Severe patient-prosthesis mismatch can be found in up to 32% of patients after a valve-in-valve procedure.50,51

In an analysis based on data from the PARTNER trial, immediate insertion of a second transcatheter prosthetic valve within the first after TAVR was an independent predictor of 1-year cardiovascular mortality (HR, 1.86; 95% CI, 1.03–3.38; P=0.041), with a nonsignificant trend toward greater all-cause mortality (HR, 1.43; 95% CI, 0.88–2.33; P=0.15).52

Very few data exist on the valve-in-valve concept for treating patients long term after TAVR. Given the results for valve-in-valve after SAVR and immediately after TAVR, the enthusiasm for this therapy in the setting of failing TAVR does not seem justified. Although the valve-in-valve concept is an interesting option for treating selected patients with degenerated bioprosthetic valves, its mere technical feasibility does not justify the use of TAVR in a younger population. Even when, and if, multiple valve-in-valve procedures become a realistic option, such a strategy must be compared with a single-stage surgical approach in a trial setting before the indications can be expanded.

Other Complications

In addition to major adverse events, paravalvular leak, and LBBB, a number of procedure-related complications have been reported in the context of TAVR. Among others, device embolization, access complications, annular or ventricular rupture, and coronary obstruction or occlusion occur.

Procedure-related vascular complications occur frequently after TAVR. In a meta-analysis including 16 studies, the rate of major vascular complications was 11.9%.29 In the transfemoral TAVR group of the GARY registry, the rate of vascular complications (15.9%) was in the same range.6 The incidence of vascular complications is significantly higher in patients who undergo TAVR compared with those who undergo SAVR (13.8% versus 2.0%; RR, 5.65; 95% CI, 3.36–9.50; P<0.00001).23 Vascular complications are associated with increased mortality.27

Coronary obstruction during TAVR occurs at a rate of 0.6% to 1% and remains a life-threatening complication (30-day mortality, 40%).53

Annular (aortic root) rupture is rare, but the combined rate of annular or left ventricular outflow tract rupture is reported to be 1.1%.27 Left ventricular outflow tract calcification and aggressive annular area oversizing are associated with an increased risk of aortic root rupture during TAVR with balloon-expandable prostheses.54 Aortic root rupture is associated with a 48% to 100% mortality.21,54

Although overly aggressive oversizing can be avoided, the rate of annular rupture has not changed over the years and remains a concern, particularly when TAVR is offered to low-risk patients.

Emergency cardiopulmonary bypass is required in ≈1.1% to 4.9% of patients undergoing TAVR, usually as a result of annular or ventricular rupture, aortic dissection, coronary occlusion, or device embolization.21,55 Emergency cardiopulmonary bypass is associated with a mortality rate of 35% to 50% (Table).21,55

Money Matters

Although TAVR is cost-effective in inoperable patients, conflicting results exist with regard to its cost-effectiveness compared with surgery in high-risk operable patients.56 For high-risk operable patients included in the PARTNER trial, the incremental cost-effectiveness ratios were well beyond the generally accepted maximum threshold.57 The currently available data do not conclusively demonstrate that TAVR is incrementally cost-effective compared with SAVR for high-risk surgical candidates because of the wide variability of incremental cost-effectiveness ratio values and probabilities of economic acceptability reported in different countries and reimbursement systems.58 Six of 9 analyses reported an incremental cost-effectiveness ratio value that would have been deemed unacceptable with the use of a US $100000 per quality-adjusted life year gained threshold, and 7 would have been deemed unacceptable with the use of a US $50000 per quality-adjusted life year gained threshold. In the United States, the total costs of TAVR and SAVR were generally similar because the higher device- and procedure-related expenses for TAVR were offset by the comparatively greater costs of hospitalization after SAVR.58 If cost-effectiveness in a (surgical) high-risk population cannot be demonstrated, it can hardly be expected in a low-risk group of patients. Low-risk patients undergoing SVR have a short (if any) stay in the intensive care unit and can usually be discharged shortly after surgery, effectively decreasing the costs for hospitalization. The costs for implants (for both SAVR and TAVR) are independent and unrelated to the underlying patient risk.

If TAVR is performed in a low-risk population, the expected long-term survival implies the need for multiple reinterventions (because of valve degeneration), thereby introducing another health economy challenge.
Principal Shortcomings of Outcome Reporting

Shortcomings of outcome reporting are not unique to but also observed in the TAVR literature. As pointed out in a meta-analysis,22 a substantial number of studies comparing TAVR and SAVR did not report outcomes based on an intention-to-treat analysis. Some excluded patients with unsuccessful implantations or periprocedural death, whereas others did not analyze crossovers from TA VR to SA VR. These reporting problems apply also to some of the national registries. Because the rate of missing data or crossovers after unsuccessful TA VR is not always known, some uncertainty about the reported outcomes remains.

Discussion

The invention of TAVR is an example of disruptive technology or innovation, a term originally coined by Bower and Christensen.59 The concept describes a new technology (TAVR) that unexpectedly displaces an established one (SAVR). Sustaining technology (SAVR) relies on incremental improvements of an existing product (eg, the introduction of a new anticalcification treatment to improve the long-term performance of a bioprosthesis) and usually does not create new markets (the market for surgical treatment of aortic stenosis is not affected by the new anticalcification treatment). On the contrary, a disruptive technology (or innovation) and the resulting business model can either create new markets (treatment of inoperable aortic stenosis) or have a disruptive impact on existing markets (Figures 1 and 4). The Bower and Christensen definition of disruptive technology reads like a blueprint for Anderson’s innovation that laid the foundation for TA VR:

Disruptive innovations are technologically straightforward, consisting of off-the-shelf components put together in a product architecture [TAVR] that is often simpler than prior approaches [SAVR]. They offer less of what customers in established markets want and so can rarely be initially used there. They offer a different package of attributes [no cardiopulmonary bypass, percutaneous access] valued only in emerging markets remote from, and unimportant to, the mainstream [standard SAVR in low-risk patients].60

According to the EuroHeart survey and other series, 30% of patients with severe aortic stenosis were refused treatment until TAVR was introduced into clinical practice. After opening the market of inoperable patients, the procedure is currently at the stage of “low-end” disruption. The performance

Table. Outcomes in High-Risk Operable Patients

<table>
<thead>
<tr>
<th></th>
<th>SAVR</th>
<th>TAVR</th>
<th>Impact on Long-Term Survival</th>
<th>Impact on Long-Term LV Function</th>
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<td>Mortality at 30 d</td>
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<tr>
<td>Stroke rate</td>
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<td>Same</td>
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<tr>
<td>Durability</td>
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<td>Unknown</td>
<td>Likely</td>
<td></td>
</tr>
</tbody>
</table>

Patient informed consent should include procedure-related risks and their impact on long-term outcomes and raise awareness for uncertainties such as durability. AI indicates aortic insufficiency; LBBB, left bundle-branch block; LOS, length of stay; LV, left ventricular; MI, myocardial infarction; SAVR, surgical aortic valve replacement; and TAVR, transcatheter aortic valve replacement.

Figure 4. A disruptive technology (innovation) such as transcatheter aortic valve replacement (TAVR) initially targets “low-end” customers who do not need full product performance (very high-risk elderly patients) or target customers who have needs that were previously unserved by existing technologies. The latter applies to patients deemed inoperable by the existing “sustainable” technology (surgical aortic valve replacement [SAVR]) and represents a new market disruption. TAVR is currently at the stage of low-end disruption (*), and the performance of TAVR (the product) starts to exceed the needs of the lower-end customer segments. At this point, technology and risk-benefit assessments are crucial to direct further market penetration. Figure derived from Christensen.60

Figure 4. A disruptive technology (innovation) such as transcatheter aortic valve replacement (TAVR) initially targets “low-end” customers who do not need full product performance (very high-risk elderly patients) or target customers who have needs that were previously unserved by existing technologies. The latter applies to patients deemed inoperable by the existing “sustainable” technology (surgical aortic valve replacement [SAVR]) and represents a new market disruption. TAVR is currently at the stage of low-end disruption (*), and the performance of TAVR (the product) starts to exceed the needs of the lower-end customer segments. At this point, technology and risk-benefit assessments are crucial to direct further market penetration. Figure derived from Christensen.60
of TAVR (the product) starts to exceed the needs of the lower-end customer segments. At this point, technology and risk-benefit assessments are absolutely crucial to directly further market penetration (Figure 4).

TAVR has proven to be a safe and efficient treatment for inoperable patients with aortic stenosis, and there is equipoise with regard to early and midterm mortality for operable high-risk patients. Before the indications of this technology are extended to a lower-risk group and younger patients, the net risk-benefit ratio needs to be evaluated. As it is the case with most disruptive technologies, a lack of refinement and performance problems exist also with TAVR. These problems materialize in a stroke rate in excess of surgery, a high rate of paravalvular leaks, a high rate of persistent LBBB after the procedure, vascular complications, and uncertain durability, all of which may impair the long-term outcomes of this promising technology.

Patient preference, often triggered by direct patient marketing and misleading advertisements by both companies and healthcare providers, has already generated a demand for TAVR outside the high-risk population. Off-label use, self-referral bias, and economic incentives continue to drive TAVR out of the corridor of current guideline recommendations and underlie the need for patient informed consent and heart team discussions as a basis for medical decision making. The potential bias that self-referral can introduce into decision making has long been recognized in the field of cardiology61 and led to the current recommendations for interdisciplinary heart teams.4 These teams can provide the appropriate framework for conducting clinical trials in lower-risk populations. These trials are necessary and timely and are currently recruiting.

Severe aortic stenosis has a pooled prevalence of 3.4% in the elderly. Under the current indications, ≈290,000 elderly patients with severe aortic stenosis are TAVR candidates, and nearly 27,000 patients become eligible for TAVR annually.62 These patients already qualify for TAVR and should preferably be served first before the indication is expanded to other patient populations without sound scientific proof of superiority.

Disclosures

Dr Falk reports receiving research grants from Boston Scientific and Phillips, receiving honoraria from Edwards and Aesculap, and serving as a consultant for Edwards and Medtronic.

References


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Response to Falk

Stephan Haussig, MD; Axel Linke, MD

Dr Falk rightfully acknowledges the excellent outcomes of conventional aortic valve replacement (AVR), even in an elderly population. In Placement of Aortic Transcatheter Valve Trial Edwards SAPIEN Transcatheter Heart Valve (PARTNER) cohort A, transcatheter AVR (TAVR) did not improve survival in operative high-risk patients. Given that the life expectancy is reduced in this population, especially because of comorbidities that are often life-limiting, it will be hard to show a survival benefit of TAVR compared with surgical AVR (SAVR) in those who are extremely sick. However, patients recovered much more quickly after TAVR and gained quality of life earlier after the intervention. This achievement is often ignored when the discussion between TAVR and SAVR comes down to a comparison of survival curves. Recently, in a patient population that was less sick on the basis of the Society of Thoracic Surgeons score compared with PARTNER A, Adams et al reported that TAVR with a self-expanding transcatheter aortic valve bioprosthesis was associated with a higher survival rate at 1 year than SAVR. This treatment effect was consistent and independent of age, sex, Society of Thoracic Surgeons score, and ejection fraction. It appears that the lower invasiveness and higher aortic valve orifice areas after TAVR might outweigh the lower level of aortic regurgitation and conduction abnormalities after SAVR, despite all present TAVR shortcomings. In addition, there was no evidence of increased stroke rates at short- or longer-term follow-up with TAVR. These data provide further evidence that TAVR might be an alternative to SAVR even in a lower-risk population. Nevertheless, results from randomized trials are required before the indications can be expanded.
Transcatheter Aortic Valve Replacement Indications Should Not Be Expanded to Lower-Risk and Younger Patients
Volkmar Falk

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