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Patient selection for TAVI in 2014: is there a justification for treating low- or intermediate-risk patients? The surgeon's view

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- aortic stenosis
- risk category
- surgical aortic valve replacement
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Abstract

The introduction of transcatheter aortic valve implantation (TAVI) has revolutionised the treatment of patients with symptomatic severe aortic valve stenosis (AS). In extreme and high-risk patients, randomised studies have shown the benefit of this new therapy. However, there are still a lot of unknowns, and the question has arisen whether it is justified to expand the indication of TAVI to other patient groups, especially intermediate- or even low-risk patients.

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Introduction

The introduction of transcatheter aortic valve implantation (TAVI) has revolutionised treatment of patients with symptomatic severe aortic valve stenosis (AS).

TAVI in inoperable patients has been shown to significantly improve survival over medical treatment, and today, in patients with severe AS and extreme operative risk, TAVI is now a class I recommendation in the most recent guidelines of ESC/EACTS[1].

In another category of high-risk patients, the PARTNER IA trial has demonstrated non-inferiority of the SAPIEN valve (Edwards Lifesciences, Irvine, CA, USA) to surgical aortic valve replacement (SAVR), and the CoreValve US pivotal trial[2] even demonstrated a significantly higher rate of survival at one year than SAVR. TAVI is now therefore considered a viable treatment alternative to SAVR in patients at high operative risk provided a multidisciplinary Heart Team has confirmed the TAVI indication and there is sufficient life expectancy.

Whilst those randomised studies show encouraging results, there is still a high early risk of death following intervention. This risk then falls to a lower level, before gradually rising above that expected in the general population. These findings diverge from surgical reports of AVR, where instantaneous risk of death is seen to be progressively less than that of the general population as patient age increases. Probably this is due to the selection of lower-risk patients, but a late influence of TAVI complications cannot be excluded. There are still risk factors for early and late mortality after TAVI that we have not identified, and there is a patient category for whom intervention may even be futile[3].

As there are still a lot of unknowns, the question arises whether it is justified to expand the indication of TAVI to other patient groups, especially intermediate- or even low-risk patients. While it could be argued that treating lower-risk patients will most likely result in improved outcomes with TAVI as well, the critical question is whether these outcomes would be similar to surgical aortic valve replacement. Why do we need the results of trials that are currently assessing surgical AVR versus TAVI for patients at intermediate risk? The PARTNER II trial has completed enrolment of the Edwards SAPIEN XT valve versus surgery, while the SURTAVI trial (surgery versus CoreValve [Medtronic, Minneapolis, MN, USA]), the UK-TAVI trial and the Nordic Aortic Valve Intervention (NOTION) trial are still enrolling patients in the intermediate risk category. These trials are costly, and yet they are still necessary for the following reasons.

Risk stratification

Risk models are essential for clinical decision making, benchmarking of clinical practices and patient selection in clinical trials. To differentiate risk categories in trials comparing TAVI versus surgical AVR, traditionally surgical risk scores like the logistic EuroSCORE I, EuroSCORE II and the STS PROM have been used. However, they predict 30-day or in-hospital mortality after surgery and are not designed nor validated to assess mortality after TAVI. Comparing two different treatments also means that certain variables may play a role in predicting outcomes for one type of therapy, but not for the other. Anatomical factors (chest radiation, femoral vessel size, coronary bypass surgery in the patient's history with mammary arteries crossing the midline, etc.) are also not included in these scores. It has also been shown that, in patients who underwent AVR, both STS PROM and EuroSCORE II overpredicted mortality[4]; classifying patients into low- or intermediate-risk categories as well, the rationale for the cut-off points for the different categories is often lacking[5]. Risk stratification usually only considers hospital mortality as an outcome, but in an elderly patient population other outcomes may be more important. Risk stratification could also mean allocation of patients according to one-year outcomes, event-free survival or outcomes in terms of quality of life or treatment costs[6]. The Heart Team, consisting of surgeons, interventional cardiologists, non-interventional cardiologists, anaesthesiologists and geriatricians, can optimise patient selection through identification of the risk/benefit ratio of surgery versus TAVI, evaluating data from randomised trials and observational registries as well as educating patients and family.

Expanding indications

Why would we already move towards lower risk patient categories when we first need to unravel the concerns involved with other indications? The following categories of patients who are at high risk for surgical treatment have not been adequately studied.

FAILING SURGICAL BIOPROSTHESIS

Valve-in-valve implantation is a heterogeneous group of procedures, performed in various surgical valves with different modes of degeneration. Survival is lower among patients with small bioprostheses and those with predominant surgical valve stenosis[7]. After surgical AVR, patient-prosthesis mismatch resulted in decreased survival rates[8], and the same can be expected for TAVI.

BICUSPID PATHOLOGY

A bicuspid aortic valve is one of the most common congenital cardiac anomalies. Due to the high risk of paravalvular regurgitation and embolisation during TAVI, patients have been excluded from randomised trials and there is little experience with this condition. Successful results, however, have been reported in select patients with predominant aortic stenosis[9]. Further studies are needed to find out which patients with bicuspid valves can be safely treated with TAVI.

PURE AORTIC REGURGITATION

Native aortic valve regurgitation is still considered a contraindication for TAVI due to the risk of insufficient anchoring of the valve prosthesis within the aortic annulus. In a small series of 43 patients treated with the CoreValve prosthesis, a device success rate of 74% was achieved. In eight patients, two valves were necessary, and nine patients had residual aortic regurgitation that was greater than mild[10]. Promising results have been achieved with a second-generation TAVI, the JenaValve (JenaValve Technology GmbH,

Munich, Germany) (n=5), currently the only valve with a CE mark for patients with predominant aortic regurgitation. Experience is limited, however, and results need to be confirmed in a larger series of patients[11].

Unresolved issues

To ensure a favourable risk–benefit ratio many of the issues below need to be addressed before moving to patients with lower surgical risk. As low- or intermediate-risk patients will have a longer life expectancy, it should be taken into account that certain complications will only have an impact and greater effect on the quality of life after a certain period of time.

PARAVALVULAR REGURGITATION

The impact of paravalvular leaks on short- and long-term mortality has been consistently reported across studies. Moderate–severe paravalvular regurgitation is an independent predictor of mortality in the postoperative period to 30 days, at one year, and at two years[12,13]. Longer follow-up will demonstrate an even more detrimental effect on cardiac function.

MYOCARDIAL INJURY

Atherosclerotic material and calcific fragments of the native valve may break off and embolise during TAVI implantation. Still, myocardial infarction rates defined by enzyme rise are rather low, ranging from 0-6%[14]. However, a recent study using cine MRI found many more ischaemic-type myocardial lesions after TAVI, most likely of embolic origin, in 18% of patients. These patients featured a significant decrease in left ventricular function at discharge. Although there was no association with in-hospital outcome, myocardial injury may have prognostic implications[15].

BLOCKING OF THE CORONARY OSTIA

A low origin of the coronary ostia, the extent of calcification of the leaflets, as well as the design of the TAVI device itself influence the chances of obstructing the coronary ostia.

CONDUCTION ABNORMALITIES AND PACEMAKER IMPLANTATION

Pacemaker implantation after TAVI is considerably more frequent than after surgical AVR[16] and associated with reduced left ventricular ejection fraction and impaired left ventricular unloading. However, it does not seem to affect two-year survival[17]. While in elderly patients the negative haemodynamic response of pacemaker implantation might be outweighed by the TAVI-related recovery of left and right ventricular performance, in younger patients, with longer life expectancy, it may influence survival at longer-term follow-up.

VASCULAR COMPLICATIONS

Vascular complications occur frequently after TAVI with an incidence of around 10%[18,19]. The reduction in sheath size and the introduction of percutaneous suture device techniques made it possible to avoid surgical cutdown to expose the femoral artery. Nonetheless, serial ultrasound evaluation of the access site is necessary to detect complications that may otherwise go undetected. Closure of the vessel, perforation, dissection or pseudoaneurysm formation of the common iliac or femoral artery are frequently reported[20].

BRAIN INJURY

Stroke after TAVI was not higher when compared to surgical AVR in high-risk patients[2]. In younger, healthier patients, however, these stroke rates after surgery are lower, while the stroke rate after TAVI might be the same, because, as in TAVI, strokes are related to the procedure itself rather than to the disease of the patient. TAVI has also been associated with subclinical brain injuries which occur more frequently than stroke. This may result from the dislodgement of atherosclerotic material during manipulation of the aorta, balloon valvuloplasty and the implantation of the prosthesis itself in the calcified aortic valve. Long-term studies are needed to learn whether these, often silent, cerebral infarcts are associated with subtle cognitive changes and increased risk of subsequent dementia[21].

MITRAL VALVE COMPLICATIONS

Low placement of the device into the left ventricular outflow tract may interfere with the movement of the anterior mitral leaflet[22], and contact-related mitral injury may occur. This would be observed with longer follow-up and may even play a role in endocarditis of the mitral valve. The contacting surface of transcatheter aortic valves may facilitate satellite infection to the anterior mitral valve leaflet[23].

ANTICOAGULATION

Antithrombotic therapy in the setting of TAVI has only been empirically determined, while the procedural risks of ischaemic stroke and major bleeding are high throughout the first month after the procedure. Following implantation, patients receive dual antiplatelet therapy (aspirin 75 mg daily plus clopidogrel 300 mg loading dose followed by 75 mg daily) for six months and, after six months, aspirin 75 mg/day lifelong. However, anticoagulation is inadvertently associated with higher bleeding complications, and carefully crafted and conducted randomised trials are needed to study the balance between the efficacy and risk of anticoagulation therapy in TAVI patients[24].

DURABILITY

Durability is the sum of all valve-related complications that occur after the patient has left the hospital; it is influenced by multiple factors. Failure rates of surgical valves should be interpreted with caution as they are most often based on reoperation-free data which is not the same as durability. As TAVI is a relatively new therapy, long-term data regarding prosthesis durability are not currently available. So far, studies have shown no significant structural degradation, leaflet thickening, calcification, thrombus formation or change in transvalvular pressure gradients from baseline to five-year follow-up[25]. In a recent study addressing valve durability, no

clinically significant deterioration in valve function was observed, but one-half of the patients who underwent TAVI because of a high or prohibitive surgical risk profile had died at a mean follow-up of 3.5 years[26]. Valve longevity in patients with high surgical risk and/or >80 years old is less of a concern; nevertheless, in patients who are at low-to-intermediate risk, durability of the TAVI device should be comparable to surgical bioprosthetic valves.

In surgical bioprostheses, the major cause of failure is related to calcification and tears of the valve cusps resulting in regurgitation or stenosis. The transcatheter heart valve is prepared, crimped and placed into the delivery system. Crimping of the valve may induce substantial structural damage to pericardial leaflets and reduce longevity[27], which may only become apparent at longer-term follow-up.

COST-EFFECTIVENESS AND REIMBURSEMENT

The unsustainable trend of rising healthcare costs necessitates careful economic evaluation of the introduction of a new technique. TAVI is a reasonable option for the extreme-risk patient with severe aortic stenosis, and offers reasonable value for the money spent on the procedure[28]. However, these results cannot be extended to TAVI in lower-risk patient populations and cannot be applied to patients who could either get surgical AVR or for other indications. In high-risk patients with severe AS, TAVI did not show a survival advantage in the Partner IA trial and only a modest improvement in the CoreValve pivotal trial[2]. There was only a brief quality of life benefit compared with surgical aortic valve replacement[29]. In intermediate risk patients, length of stay and complications after surgery will be lower, and TAVI needs to demonstrate whether it is still economically attractive[30].

In Europe many intermediate-risk patients are already treated with TAVI; however, without a randomised trial, we will never be able to answer some of the questions raised above. There are lessons that we can learn from the rapid expansion of percutaneous interventions (PCI), especially after the introduction of drug-eluting stents. While many patients with complex coronary artery disease were treated with PCI, later randomised studies showed a higher than expected rate of adverse events with PCI compared to coronary surgery[31]. Quality of life benefits will need to be proven in order to justify expansion of TAVI indications. Given our current state of knowledge, if there is clinical equipoise in the intermediate- or low-risk patient, this should be tested within the context of a clinical trial.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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