

Percutaneous pulmonary and aortic valve insertion in Belgium: Going for conditional reimbursement or waiting for further evidence?

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Objectives: The aim of this study was to assess current evidence supporting the use of percutaneous heart valves (PHV) in degenerative aortic valve and congenital pulmonary outflow tract disease, as compared to conservative medical therapy or traditional surgical valve replacement.

Methods: A systematic review of the literature on PHV was performed.

Results: No randomized controlled trials (RCT) on PHV have been published so far. Only observational data from series and data presented at cardiology meetings are available. Both percutaneous aortic valve (PAV) and percutaneous pulmonary valve (PPV) seem feasible in the hands of an experienced team. Safety, however, seems to be a problem in PAV, as shown by the high 30-day and 6-month mortality rates.

Conclusions: Due to safety concerns, PAV reimbursement is not recommended and patients should only be subjected to PAV insertion within the boundaries of an RCT. In contrast, PPV implantation seems to be a safe and promising technology for which reimbursement under strict conditions may be recommended.

Keywords: Heart valve prosthesis, Heart valve prosthesis implantation, Technology assessment, Biomedical

Percutaneous Aortic Valve

Aortic stenosis (AS) is the most common valvular heart disease in adults and generally is degenerative in origin, resulting from a progressive age-dependent build-up of calcium in the aortic valve. Its prevalence is strongly related to po-

pulation ageing, and as such is expected to represent an increasingly important public health problem (29). In patients with AS, a narrowing of the aortic valve opening creates increased resistance to the flow of blood from the left ventricle to the aorta. This may lead to symptoms, heart failure, and in symptomatic patients with a severe stenosis, to sudden death.

Pharmacological treatment of patients with symptomatic AS can result in a temporary alleviation of symptoms. Cur-ing AS, however, requires surgical aortic valve replacement (AVR), which is the gold standard treatment for AS (1). This is a time-honored technique, which has produced excellent

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Table 1. Timeline of Patients with Tetralogy of Fallot in Whom Early Complete Repair Is not Feasible

Repair	Initial revalving	Replacement of conduit (redo)	Redo	Redo
		stenting PPV? ^a		
Age 0–8 months	Age 10–20 years	Age 20–30 years	?	?
Surgical repair of obstructive lesions of the RVOT early in life can be life-saving, but creates pulmonary valve incompetence	Later on, patients need the placement of a (homograft) valved conduit	The lifespan of homografts is much shorter than that of the patients receiving them, thereby making future surgical reintervention(s) unavoidable		

^aPPV? indicates conditions where percutaneous pulmonary valve (PPV) insertion may be appropriate. Ages may vary widely between patients.

RVOT, right ventricular outflow tract.

results in an estimated one million patients over the past four decades. Experienced surgeons can perform it with single-digit mortality, even in octogenarians (2). These patients also present with significant comorbidities that hitherto sometimes impeded surgeons to proceed to surgical correction of the valvular disease because of the expected high perioperative mortality rates in frail and elderly high-risk subjects. This observation has led to the development of percutaneous aortic valve (PAV) technology, which by its less invasive nature, is believed to represent a safer treatment modality for these elderly patients.

The first human PAV implant has been performed by Cribier et al. in April 2002 (8). Since Cribier's first experiences, several devices have been developed and at least twenty types are currently being tested at various stages in humans, in animal models, or in laboratories (13). Currently, two different PAVs have received European CE marking and are available for clinical use: the Edwards LifeSciences and the CoreValve PAV. In contrast to the Edwards type of PAV, which is deployed by means of a balloon, the CoreValve is self-expandable. Up to 2008, reportedly more than 1,000 Edwards PAVs and 1,400 CoreValve PAVs have been implanted worldwide in humans (30). This assessment on PAV is limited to these PAV types.

Percutaneous Pulmonary Valve

Some types of congenital heart diseases, such as malformations of the right ventricular outflow tract (RVOT) in tetralogy of Fallot, require surgical correction early in life (Table 1). For some patients, this early repair only represents a temporary solution, and additional surgery later on, is needed. This may consist in the construction of a valved conduit between the heart and the pulmonary artery. Because of outgrowth and/or degeneration of these valved conduits, patients may have to undergo one or more repeat surgical interventions. In most cases, the repeat intervention is performed, not so

much for symptomatic reasons, but rather to prevent the occurrence of heart failure and potentially lethal ventricular arrhythmias later in life. To postpone repeat surgery or to decrease the label of surgical redo interventions, percutaneous pulmonary valve (PPV) insertion has been developed. Because of vascular dimensions needed to percutaneously introduce the device, the technique currently cannot be used in the very young, and patients have to weigh at least 20 kg (18). PPV insertion was first reported in the year 2000 (4).

Published experience is essentially limited to one PPV type, the "Melody" valve manufactured by Medtronic. Until May 2008, 556 Melody PPVs had been implanted worldwide (30).

This assessment is part of a health technology assessment (HTA) report made by the Belgian Health Care Knowledge Centre (KCE), an independent semigovernmental institution, to support policy makers (30).

METHODS

To find previously published HTA reports, the Centre for Reviews and Dissemination (CRD) and International Network of Agencies for Health Technology Assessment (INAHTA) databases were searched in May 2008. Next, in June 2008, the Cochrane, CRD, Medline, and Embase databases were searched for systematic reviews and primary studies on percutaneous heart valves (PHVs). The searches were repeated in December 2008. More details on the applied search strings are available in the full HTA report (30). Data presented at meetings, those provided by manufacturers and information retrieved from grey literature have not been included in our formal literature survey because of the non-peer-reviewed character of the data. They will, however, be taken into account in the discussion of the subject.

Before summarizing the evidence, the regulatory status for medical devices in the United States and European Union (EU) is explained.

Regulatory Status

The regulation of medical devices is different in the United States as compared to the EU, especially the requirements for bringing devices on the market. In the United States, medical devices are classified into classes depending on their intended use, the indications for use, and potential risks associated with their use. In the United States, there are three classes for which regulatory control increases. Most Class I devices are exempt from Pre-market Notification (510(k)); most Class II devices require Pre-Market Notification 510(k); and most Class III devices require Pre-Market Approval (PMA). An investigational device exemption (IDE) can be provided to allow the investigational device to be used in a clinical study to collect safety and effectiveness data required to support a PMA application or a Pre-Market Notification submission to the Food and Drug Administration (FDA). An IDE was granted for the Edwards-Sapien PAV for use in the currently ongoing pivotal randomized controlled trial (RCT), the PARTNER (Placement of AoRTic TraNscatheter Valve Trial) trial. This trial should be distinguished from the "PARTNER EU" study that is a single arm, prospective post-market registry, conducted in the EU (26). To avoid ambiguity, the U.S. based RCT often is referred to as the "PARTNER US" or the "PARTNER IDE" trial. Currently, no RCTs are identified with the CoreValve.

In the United States, an exemption on the effectiveness requirements is possible for a Humanitarian Use Device (HUD). A HUD is a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year. FDA may authorize a company to market their HUD by approving a Humanitarian Device Exemption (HDE), which is similar to a PMA application, but exempt from the effectiveness requirements (28). Reasonable evidence of safety and only probability of benefit are required for this exemption (40). The HUD-label was assigned for the Melody PPV for use in patients with specific clinical conditions. Medtronic submitted a request for HDE on August 28, 2008 (personal communication). The procedure currently is still running.

In Europe, medical devices are classified in four classes: class I (low risk), II a (medium risk), II b (elevated risk), and III (high risk) (14). The higher the classification, the more elaborate the level of the required assessment will be. Cardiac devices are placed in class III (40). In this class, a CE mark for marketing can only be affixed by the manufacturer after approval of the "Design Dossier" by a Notified Body, designated by a Competent Authority. The CE mark denotes a formal statement by the manufacturer of compliance with the directives' requirements. The Medtronic Melody PPV received CE marking in October 2006. The CoreValve PAV received CE marking in May 2007, while the Edwards Sapien PAV has been granted a CE marking in September 2007 for its transfemoral device and in December 2007 for its transapical device.

The FDA's PMA requires the demonstration of a medical device's clinical effectiveness as a precondition for marketing. This is not the case with CE marking (31). The technical CE label does by no means provide evidence for the clinical effectiveness nor the clinical safety and potential long-term adverse events in the patient populations concerned. For class III implants, clinical trials should be performed to demonstrate that the "essential requirements" (i.e., characteristics and performance of the device) are met, unless there is adequate justification to rely on existing clinical data. This requirement is part of the assessment of the technical file by the Notified Bodies. It can be regarded as a necessary first step to guarantee technical safety and good manufacturing of a device, but its value in health technology assessment for health insurance is limited (31).

RESULTS

Figure 1 shows the selection procedure of relevant papers. In 2008, three HTAs have been published on PAV (17;24;38) and two on PPV (20;23). The studies identified in these reports were included in our search results. No RCTs on PHV have been published so far. All papers retrieved were case series. Of twenty-five reports on PAV, ten were "single case" reports. Because of their obvious anecdotal nature, these "single cases" will not be mentioned further. In the update of our search, another two articles on PAV were identified (11;27). Of the twelve articles on PPV, four were "single case" reports. From the remaining eight papers on PPV, one reported three cases, and the remaining seven papers all originated from a single operator, that is, Philipp Bonhoeffer, who treated his first patients in Paris and later on in three different centers in London. The most recent paper from this group including the largest population (155 patients) will be discussed in more detail.

PAV

Table 2 represents the seventeen articles on the PAV that are considered in this review.

There are no data on the performance of PAV based on RCTs. Only observational data from series, published in peer reviewed journals (300 cases), and data presented at cardiology meetings (>1,600 cases) are available (30). Published case series indicate that PAV insertion is feasible in the hands of experienced operators in up to 90 percent of eligible patients. Some authors even reported success rates up to 100 percent, however, these occurred in small population series. Nevertheless, PAV insertion in these populations seems to be a risky intervention with 1-month mortality rates from 11.1 percent to 25 percent in transfemoral retrograde PAV insertion and 6.6 percent to 17.5 percent in transapical series. Unpublished data even report wider uncertainty with both superior and inferior results (30). In these patients, it is uncertain what their mortality would have been if they had been operated conventionally or treated medically.

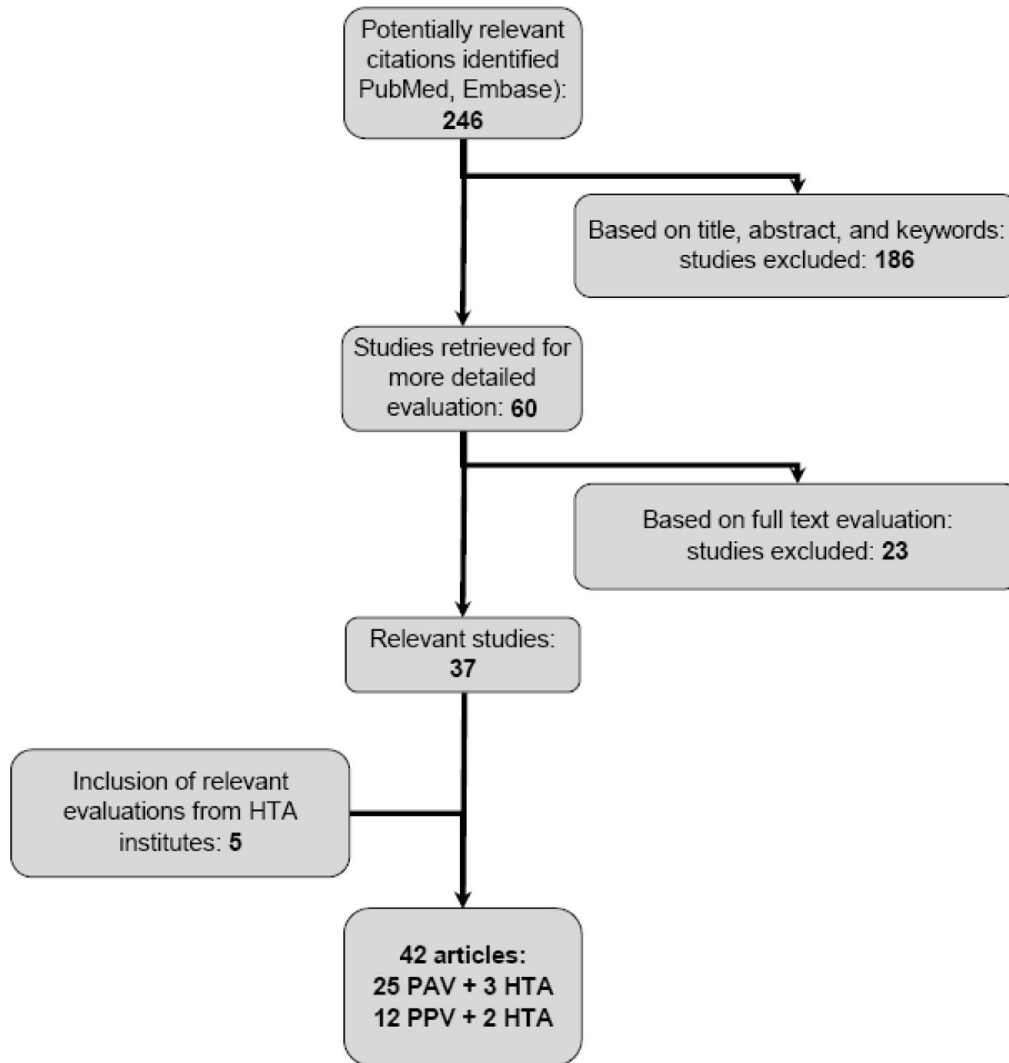


Figure 1. Literature search. HTA, health technology assessment.

The short-term efficacy of PAV seems to be good. Patients in whom a PAV has been successfully inserted are reported to experience an improvement in their New York Heart Association (NYHA) functional class (from NYHA III to NYHA I/II), in accordance with an improved valvular function by echocardiography and Doppler (30). No studies reported quality of life (QoL) outcomes, and, therefore, it is not clear what the real impact of PAV would be on a generic measurement of QoL. Nevertheless, these patients have additional (severe) comorbidities that affect their QoL, even after successful PAV insertion.

Few 6-month survival data have been published. The 6-month mortality was very high (61 percent) in the antegrade (transvenous) approach, however, this method has mostly been abandoned. Two studies mentioned a 6-month mortality rate with the latter approach of 18 percent and 25 percent (11;37). This was even 26 percent and 41 percent in transapical series (27;35). Again, including case series presented at 2008 cardiology meetings broadens these reported

high mortality rates, ranging from 10 to 21.7 percent in trans-femoral series and 26.1 to 45.0 percent in transapical series (30).

Long-term (>1 year) performance is related to the impact of a potential residual aortic regurgitation resulting from a suboptimal positioning of the PAV, and to the service life of the valve. There is, however, practically no data on the long-term clinical effectiveness of PAV insertion as compared to medical therapy or conventional surgery.

PPV

Table 3 summarizes the feasibility and safety data from Bonhoeffer’s series on PPV (21).

There are no data on the performance of PPV insertion based on RCTs. Published data essentially are restricted to case series originating from one single operator (Philipp Bonhoeffer, Paris and London). In his hands, PPV insertion is feasible in almost all patients selected for the procedure.

Table 2. Feasibility, Safety, and Survival Data Extracted from Published Case Series of PAV

Study no.	Reference	Time window	n	Age	Logistic EuroSCORE	Success	30-day mortality	6-month mortality
Edwards, transfemoral, ^a antegrade ^b								
1 ^c	Cribier (9)	Apr 2002–Aug 2003	6	75	NA	83	50	NA
2	Cribier (10)	Aug 2003 – NA	36	80 ± 7	NA	75	22.2	61.1
2bis	Eltchaninoff (13)	2003–2005	36	80 ± 7	NA	75	22.2	61.1
3 ^c	Sack (25)	June 2005–July 2005	2	NA	>20%	100	0	NA
Edwards, transfemoral, ^a retrograde								
4	Webb JG (36)	Jan 2005–July 2005	18	81 ± 6	26.2 ± 13.1	77.8	11.1	NA
4bis	Webb JG (37)	Jan 2005 – NA	50	82 ± 7	28	86	12	18
5	Descoutures (11)	Oct 2006–Apr 2007	12	85 ± 6	31.1 ± 14.4	83.3	25	25
Edwards, transapical ^a								
6 ^c	Lichtenstein S (19)	Oct 2005 – NA	7	77 ± 10	7-66 ^d	100	14.3	42.9
6bis ^c	Ye J (39) ^e	Oct 2005 – NA	7	77 ± 10	7-66 ^d	100	14.3	42.9
7	Walther T (34)	Feb 2006–Sep 2006	30	82 ± 5	27.1 ± 12.2	96.6	6.6	NA
7bis	Walther T (35)	Feb 2006–March 2007	50	82.4 ± 4.6	27.6 ± 12.2	94	8	26.1
8	Walther T (33)	Feb 2006–Oct 2006	59	81.4 ± 5.8	26.8 ± 13.5	93.2	13.6	NA
9	Svensson LG (27)	Dec 2006 – NA	40	83 ± 7.5	35.5 ± 15.3	87.5	17.5	41.3
CoreValve, transfemoral, ^a retrograde								
10	Grube E (15)	Feb 2005–Nov 2005	25	80.3 ± 5.4	10.97 (19.90–9.20) ^f	84	20	NA
11	Grube E (16)	Aug 2005–Feb 2007	86	82.2 ± 5.9	21.7 ± 12.6	88.4	11.6	NA
11bis	Marcheix B (22)	Dec 2005–Aug 2006	10	81.3 (64–85)	32 (21–40) ^f	100	20	NA
11bis	Berry C (3)	March 2005–Aug 2006	11	81.8 ± 6.8	36 (5–48) ^f	100	18.2	NA

^aTransfemoral versus transapical: After predilatation of the native stenotic aortic valve, in the *transfemoral approach*, the percutaneous aortic valve (PAV) is advanced from the femoral artery, over a guidewire, through the native valve. The suitability for patients to be treated with a PAV is restricted by aortic annulus dimensions and depends on the accessibility of a patient’s arterial tree as well. The access can, for example, be rendered impossible due to severe iliofemoral atheromatous disease, a problem that has been overcome by an alternative procedure, the *transapical approach*. Here, PAV delivery directly occurs from the left ventricular apex, obviously involving a mini-thoracotomy. Patients treated by the transapical approach have a higher operative risk than those in whom a transfemoral approach is not hindered by severe atheromatous vascular disease.

^bThe antegrade (transvenous) approach of the aortic valve has mostly been replaced by the retrograde (transarterial) approach.

^cThe results from series with less than 10 patients are included in this table for completeness. However, they will not be included in our discussion due to the large uncertainty surrounding the outcomes.

^dRange.

^eThe data on mortality after the first month were only reported in the paper by Ye.

^fMedian and interquartile range.

Table 3. Feasibility and Safety Data on Melody PPV Implantation (21)

Reference	n	Median age (range)	Immediate success	Procedure related mortality	30-day survival	Survival
Lurz (21)	155	21.2 (7-71)	150 (97%)	2/155 (1.3%)	154/155 (99.4%)	median follow-up 28 months: 4 deaths

The mortality risk of PPV insertion as reported in his most recently published series is very low (1.3 percent) (21). The incidence of procedural complications fell from 6 percent in the first cohort of fifty cases to 2.9 percent in the second cohort of 105 patients.

The short-term (median follow-up 28 months) efficacy of PPV is good. Patients in whom a PPV has been successfully inserted have an adequate valvular function by echocardiography and Doppler. In a cohort of 105 patients, a redo-valve implantation was needed in 13 percent of cases, within a follow-up period of 0–40 months.

The optimal timing of the procedure to prevent right ventricular failure and fatal ventricular arrhythmias is unknown. The long-term effectiveness as compared to a traditional strategy (watchful waiting until surgery is deemed

necessary) is also unknown, and there are no data on the service life of the implanted device.

Discussion

An overview of our findings on the appropriateness, feasibility, safety, and clinical effectiveness of the PAV and PPV implantation procedure are given in Table 4.

PAV

There are several case reports of PAV in highly selected patients where surgery reportedly was no option, and where medical treatment would probably have resulted in demise in short-term. In some published case reports, the procedure resulted in a very significant to spectacular improvement of

Table 4. Appropriateness, Feasibility, Safety, and Effectiveness of PHV Insertion

Percutaneous aortic valve insertion (PAV)						
	Procedure			Clinical effectiveness		Cost-effectiveness
	Appropriateness	Feasibility	Safety	Early	Late	
Device	Unknown; depends on effectiveness of PAV as compared to conventional surgery	Feasible in 88–96% of attempts in the hands of experienced team	Safety as compared to surgery unclear; 30-day mortality 10–15% in the hands of experienced team;	Short-term hemodynamic and clinical performance good	Long-term durability unknown (but a lesser issue, given the limited life expectancy of eligible patients)	Lack of input data precludes reliable calculation of ICERs
Patient	Choice depends on patient's preference whether to opt for conservative treatment or for correction of the valvular dysfunction (by any means)		6-Month mortality 20–30%	Unknown: as compared to surgery or medical therapy, it depends on comorbidity related QoL and comorbidity related life expectancy		
Percutaneous pulmonary valve insertion (PPV)						
	Procedure			Clinical effectiveness		Cost-effectiveness
	Appropriateness	Feasibility	Safety	Early	Late	
Device	Unknown; depends on effectiveness of PPV as compared to conventional surgery	Feasible in 97% of attempts in the hands of one single operator	Early mortality 1,3% in single operator experience	Short-term hemodynamic performance good	Long-term durability of the valve unknown	Lack of input data precludes reliable calculation of ICERs
Patient	Conservative treatment is no option in symptomatic patients; in asymptomatics, timing of the intervention (by any means) is unclear		Long-term patient survival unclear	Long-term effectiveness in postponing surgery unknown		

the patient (7). These cases are typically used to promote the procedure in these highly selected cases. However, from these indications have been broadened to patients where surgery in adequate hands probably could have achieved a similar or better result at a lower risk and lower cost. However, it is not clear for which patients PAV is an appropriate alternative as compared to a conservative medical therapy or conventional surgery. Currently available data suggest that PAV insertion is feasible and provides at least short-term (6 months to 1 year) hemodynamic and clinical improvement. However, in patients that are currently considered for the procedure, life expectancy and QoL are not only determined by the aortic valve disease as such, but also depends on the comorbid conditions and obviously on the age of the patient.

Safety issues, demonstrated by a 30-days mortality rate of 6.6 percent to 25 percent in published case series, represent a major drawback for implementation of this technology. "High surgical risk" and "operability" status are poorly defined concepts and complicate the selection of patients and the interpretation of outcomes reported in case series. The operability of patients is based on clinical judgment by the clinician, supplemented with information obtained from an operative risk score—very often the EuroSCORE (European System for Cardiac Operative Risk Evaluation). High-risk indicators include, among others, advanced age, chronic obstructive pulmonary disease, reduced left ventricular function, renal failure, diabetes mellitus, and recurrent neurologic insults. Although it reflects only a limited label of surgical risk factors, the EuroSCORE risk score is commonly referred to in papers related to PAV insertion. It was introduced in 1999 to predict surgery related mortality risk (5). This risk model is used for any cardiac surgery, and is not specifically designed for aortic valve replacement (2). For a given patient, the EuroSCORE reflects the predicted operative mortality, although for patients considered at the highest risk, the EuroSCORE may overestimate the surgical risk (12;35) This has been confirmed in a recently published evaluation in a surgical series from the Mayo Clinic where an estimated 30-day mortality of 23.6 percent among 399 high-risk patients sharply contrasted with an observed mortality of 5.8 percent (6). Therefore, comparing the EuroSCORE predicted mortality in the population receiving PAV with their observed mortality (and concluding mortality is probably reduced) may be misleading. The case series with a lower EuroSCORE than 23.6 percent even had higher observed mortality rates than 5.8 percent. This suggests that patients with AS that are considered at high risk for conventional AVR, may actually present lower mortality rates if treated surgically than if treated by means of PAV insertion.

Six-month mortality of patients treated by PAV is very high, and ranges from 18 percent to 41 percent in published case series (excluding the antegrade approach and small (<10) patient series) and from 10 percent to 45 percent in nonpublished case series, questioning the appropriateness of this procedure. Presently, the intervention's cost-

effectiveness cannot be reliably calculated because no objective input data are available.

These observations reinforce the contention that RCTs are badly needed to clarify the performance of PAV insertion. Fortunately, the regulatory status in the United States resulted in the PARTNER IDE trial. The aim of the study is to evaluate the safety and efficacy of transapical and transfemoral delivery and implantation of the Edwards Sapien PAV in symptomatic adult patients with severe valvular aortic stenosis, who are high-risk candidates for routine open heart surgery. In a first cohort that is constituted of patients at high operative risk randomized to transfemoral PAV, transapical PAV, or conventional surgery, the primary outcome is freedom from death at 1 year (noninferiority). The second cohort is composed of inoperable patients who are randomized to transfemoral PAV or to medical treatment. Here, the primary end point is overall survival (superiority). QoL measures would be taken at baseline, 30 days, 6 months, and 1 year. This ongoing RCT is expected to clarify (i) if patients that are inoperable are better off with PAV than with medical treatment, and (ii) if patients at high risk for surgery have no higher risk with PAV than with conventional AVR.

PPV

In contrast to AS (in high-risk elderly people), a conservative medical treatment is no option in symptomatic patients with a degenerated pulmonary valved conduit. The feasibility and safety of PPV insertion is excellent, at least in the hands of one operator. Short-term hemodynamic and clinical performance is good.

The timing of the procedure in asymptomatic patients, the service life of the device and its ability to postpone or prevent the occurrence of heart failure and fatal arrhythmias later in life remains unknown. Data from RCTs, however, are not available and, to our knowledge, no RCT has been planned to assess the efficacy of this promising technology.

Policy Recommendations

Our policy recommendations are mainly based on what we understand as being a promising emerging technology. Two conditions should be fulfilled. First, the new technique should be at least as safe compared with comparator procedure(s). Second, it should be at least as efficacious compared with comparator procedure(s) or efficacy is not yet sufficiently determined because it is an emerging technology (32). With currently available evidence, the safety issue is especially a problem for PAV.

PAV

A reimbursement of the PAV can currently not be defended because of patient safety concerns, and a poorly defined target population. Published data are not convincing that the procedural mortality risk related to PAV insertion is lower than the risk incurred by conventional surgery in comparable

patients. Moreover, it is unclear which patients might benefit from the technology, because clinical effectiveness not only depends on the natural history of the aortic stenosis but also on the patient's life expectancy related to advanced age and comorbidities. The very high 6-month mortality rates render the appropriateness of the procedure questionable.

This recommendation can be considered up-to-date as long as no data from an ongoing RCT have become available. For ethical reasons, patients should only be subjected to PAV insertion within the boundaries of an RCT. The decision whether to reimburse PAV technology is to be reconsidered when the results of the ongoing RCT become available. If this RCT provides evidence on safety and effectiveness of the PAV, its acceptability (cost-effectiveness) and affordability (budget impact) need to be assessed.

The medical community should be well informed that the assignment of a European CE marking does not indicate that a device is safe for clinical use. It is desirable that a continuous monitoring is performed, at least on a national, preferably on a European level, for (new) implants for which clinical safety is not proven. This would enable government to intervene if necessary and ensure the patient's safety.

PPV

Although only a limited label of patients are eligible for PPV insertion (suggesting a relatively small budget impact), a reimbursement decision should ideally be based on evidence from an RCT. This is, however, not available. RCTs are needed to obtain hard evidence on the optimal timing and the appropriateness of PPV insertion as an alternative for the current strategy, that is, "watchful waiting until surgery is deemed necessary." An RCT devoted to these issues would require a follow-up of many decades and may, therefore, be unrealistic.

However, case series suggest that PPV is at least as safe as surgery. Therefore, in combination with the uncertainties surrounding the clinical effectiveness, reimbursement for PPV can be considered, but should be mandatory under strict conditions. These conditions should include, among others, a clear description of eligible patients, necessary skills to perform the procedure, selection of centers where the intervention can be performed, and so on. Furthermore, the price of the device, which should be more transparent, could be discussed before agreeing on this conditional reimbursement. With this conditional reimbursement, every case should also be well documented in a registry. Every year, a re-evaluation should be undertaken to assess procedure-related mortality and the short-term effectiveness of the device. Based on currently available evidence, this conditional reimbursement would not endanger the safety of eligible patients and allow the guided entrance of a promising emerging technology on the market.

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