Percutaneous Aortic Valve Implantation: Early Clinical Experience and Future Perspectives

Danny Dvir MD[1], Abid Assali MD[1], Hana Vaknin MD[1], Alik Sagie MD[1], Yaron Shapira MD[1], Alexander Battler MD[1], Eyal Porat MD[2] and Ran Kornowski MD[1]

Departments of [1]Cardiology and [2]Cardiothoracic Surgery, Rabin Medical Center, Petah Tikva, and Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

ABSTRACT: The incidence of aortic valve stenosis is growing rapidly in the elderly. Nonetheless, many symptomatic patients are not referred for surgery usually because of high surgical risk. Unfortunately, percutaneous balloon valvuloplasty is unsatisfactory due to high recurrence rates. In 2002, Cribier and colleagues were the first to describe percutaneous aortic valve implantation in a patient, opening a new era of aortic stenosis management. In the present review we report a patient treated by this novel method, discuss and assess how it is implanated, report the findings of studies conducted to date, and suggest future directions for percutaneous treatment of aortic valve disease.

IMAJ 2009;11:244–249

KEY WORDS: percutaneous aortic valve intervention, aortic stenosis

Aortic valve stenosis is the most significant valvular disease in the western world, and its incidence is expected to grow with the continuing increase in longevity [1]. Severe aortic valve stenosis is associated with severe morbidity and death within 2 to 3 years of symptom onset, and its accepted treatment is aortic valve replacement. However, according to the Euro Heart Survey up to one-third of affected patients who meet these criteria are not referred for surgery. This is probably in response to epidemiological findings of a 5–15% mortality risk for valve surgery in elderly individuals with significant co-morbidities [2,3]. As yet, no alternative therapy has proven beneficial in this patient population [4].

Percutaneous treatment of aortic valve stenosis could potentially lessen the risk of surgery-related complications of general anesthesia, thoracotomy and cardiopulmonary bypass. Unfortunately, percutaneous balloon valvuloplasty is unsatisfactory due to high recurrence rates within months [5-7]. In 2002, Cribier et al. [8] described the first use of percutaneous aortic valve implantation, launching a new era of aortic stenosis management.

PATIENT DESCRIPTION

An 87 year old man with known ischemic heart disease presented with deteriorating functional capacity secondary to weakness and dyspnea. His medical history revealed coronary bypass surgery performed 10 years previously and the presence of many risk factors for atherosclerosis, including diabetes mellitus, hypertension and dyslipidemia. He also had several major co-morbidities: namely, chronic obstructive pulmonary disease, partial blindness due to severe bilateral macular degeneration, polymyalgia rheumatica, and anemia secondary to chronic inflammatory disease.

On physical examination at admission, a 3/6 systolic murmur was heard at the base of the heart. Echocardiography revealed good systolic left ventricular function. There were significantly high gradients over the aortic valve (101/62 mmHg). The aortic valve had three leaflets and a calculated area of 0.55 cm^2. The diagnosis was severe aortic stenosis. Other findings were only mild aortic regurgitation and absence of dilatation of the ascending aorta. Mild pulmonary hypertension was documented as well. Angiography demonstrated patent bypass vessels, with no significant change in the native coronary vessel disease from the previous angiogram. Aortography revealed a heavily calcified porcelain-ascending aorta.

The patient was considered a very poor candidate for conventional aortic valve replacement surgery owing to his relatively old age, the previous cardiac surgery, and presence of a porcelain aorta, significant pulmonary disease, and limited rehabilitation capacity due to partial blindness. The euroSCORE predicted mortality was 20.4%, and the Parsonnet score was 36%.

We therefore evaluated the patient for suitability for percutaneous aortic valve implantation. Transesophageal echocardiography showed an aortic valve annulus of 23 mm, and computed tomography angiography showed a slightly horizontal cardiac alignment (45–50° between the horizontal and valve planes). There was evidence of severe aortic valve calcifications and calcifications along the thoracic and abdominal aorta. However, the peripheral vessels were wide: the abdominal aorta measured more than 18 mm in diameter, and the right

and left common iliac arteries more than 10 mm.

The patient underwent percutaneous aortic valve implantation in November 2008, several months after diagnosis. The procedure was performed under general anesthesia and continuous TEE monitoring by a multidisciplinary team of experts in echocardiography, intensive care, vascular surgery, radiology, cardiothoracic surgery, and invasive cardiology. At the beginning of the procedure a temporary pacemaker was inserted to allow for rapid pacing. Following a surgical cut-down in the groin, several balloon inflations were performed at the aortic valve. Thereafter, a 26 mm Edwards-Sapien balloon-expandable aortic valve (Edwards Inc., Irvine, CA, USA) was delivered through a 24 Fr introducer sheath [Figure 1A], and the balloon-valve complex was inflated under rapid ventricular pacing (220 Hz) [Figure 1B]. Fluoroscopy and aortography revealed that the valve was in the exact position, with no paravalvular leakage, and the coronary ostia were open [Figure 1C and D]. A decrease in the aortic valve gradients was noted on echocardiography, from 101/62 mmHg to 33/16 mmHg and valve area increased from 0.55 cm^2 to 1.7 cm^2. The vascular access was closed surgically.

The patient was transferred to the intensive care unit, and extubation was performed 2 hours later. One day after the procedure the patient was able to walk. There was no evidence of significant vascular or hemorrhagic complications, or of arrhythmias or conduction disturbances. The patient was discharged from hospital 5 days after the procedure in excellent condition, with early evidence of significant clinical improvement. This improvement continued during 4 months of clinical and echocardiographic follow-up.

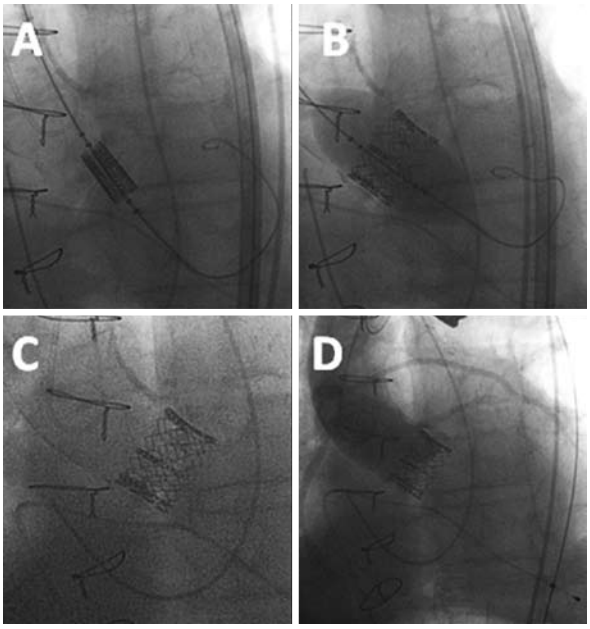

Figure 1. Fluoroscopic images during percuatneous valve implantation. Note the heavily calcified porcelain aorta. **[A]** A 26 mm Edwards-Sapien valve in closed position inside the aortic valve. **[B]** Balloon inflation of the aortic valve. **[C]** The valve after implantation. **[D]** Post-implantation aortography with only minimal aortic regurgitation.

Percutaneous treatment of aortic stenosis holds promise for providing symptomatic relief and probably longevity for patients who are ineligible for surgery

PERCUTANEOUS AORTIC VALVE BALLOON VALVULOPLASTY

Balloon valvuloplasty for the treatment of aortic valve stenosis was introduced in 1985 [9]. It eventually became an accepted procedure for children with stenosis secondary to congenital valve malformation. In adults, however, in whom stenosis is usually secondary to degenerative calcification of the valve leaflets, the enthusiasm with which the technique was initially met decreased considerably after publication of the Mansfield Registry results in the early 1990s [10]. Overall, the improvement in hemodynamics after balloon valvuloplasty was found to be suboptimal, since valve diameters after the procedure are rarely larger than 1.0 cm^2. Moreover, the complication rate on the first day after the procedure approaches 25%, and the mortality rate during hospitalization ranges from 8% to 14%. Early recurrence is high as well [5,6]. The 2006 American College of Cardiology/American Heart Association clinical guidelines list balloon valvuloplasty as a class IIb indication in hemodynamically unstable patients who require a "bridge" to aortic valve replacement. However, even in this setting, surgery is considered the treatment of choice [11]. The percutaneous approach has also been suggested as a palliative option in patients who are not referred for surgery because of serious co-morbidity. Therefore, it comes as no surprise that aortic valve balloon valvuloplasty is not routinely performed in most catheterization centers.

PERCUTANEOUS AORTIC VALVE IMPLANTATION

Non-invasive aortic valve implantation was designed to overcome the disadvantages of balloon valvuloplasty. In the early 1990s Andersen et al. [12] used a porcine model to demonstrate the durability of an aortic valve implant mounted within a stent and compressed on a balloon catheter. In contrast to aortic valve replacement in which the damaged valve needs to be removed first, the implant could be placed inside the calcified native valve. In the first percutaneous valve implantation procedure reported in humans, Bonhoeffer and co-workers [13] implanted a bovine jugular vein valve into a stenotic pulmonary valve. The implantation of an aortic valve, however, is more complicated because of the risk of disturbing the flow to the coronary vessels, distal migration

TEE = transesophageal echocardiography

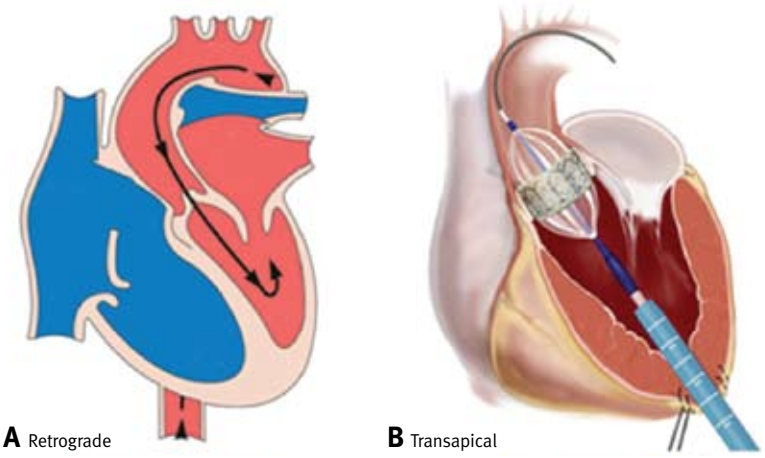

Figure 2. Illustration of common approaches for percutaneous aortic valve implantation. **[A]** Retrograde approach. **[B]** Transapical approach.

of the valve complex, and paravalvular leak between the implanted and native valve. It was only in 2002 that Cribier and team [8] performed the first human PAVI . That first procedure was performed as a last resort in a 57 year old patient with severe aortic stenosis who presented with cardiogenic shock one week after failed balloon valvuloplasty. Aortic valve replacement was contraindicated in this case because of significant co-morbidity. The procedure led to dramatic clinical improvement, and good function of the implanted valve was sustained throughout the 4 month follow-up until that patient's death from a non-cardiac cause.

Three PAVI approaches have been proposed.

- **Antegrade approach:** The initial PAVI procedures were performed via the antegrade approach under mild sedation [8,14,15]. A 24 Fr catheter is introduced via the femoral vein and directed to the right side of the heart. Trans-septal puncture and dilatation are performed, and the catheter is delivered to the left atrium and through the mitral valve to the left ventricle, crossing the aortic valve antegradely. The advantages of this approach include passage through wide veins with less limitation in patients with peripheral arterial disease and delivery of the system through the usually less damaged ventricular side of the valve, easing its placement. However, the antegrade approach is prone to complications, especially mitral valve displacement and consequent regurgitation, and it may not be applicable to the practicing surgeon. Physicians require a high level of expertise to perform the septal puncture and to pass the system through three different cardiac chambers. Thus, the antegrade approach for PAVI is no longer in clinical use.
- **Retrograde approach:** Today, this is the preferred approach [16]. A catheter is delivered through the femoral artery and directed to the aortic side of the aortic valve [Figure 2A]. This approach has several limitations as well. The delivery through peripheral arteries poses a risk of dangerous vascular complications such as dissection or arterial rupture, limiting the technique to patients without significant peripheral artery disease. Moreover, the need to transfer the large system through the ascending aorta could increase the risk of stroke due to atheroembolism. However, the retrograde approach is less technically cumbersome than the antegrade approach and is associated with a much shorter procedural time (1–2 vs. 2–4 hours). Recently, some experienced surgeons have been performing the retrograde approach even without TEE guidance.

After both the antegrade and retrograde procedures, patients remain under intensive care until hemodynamic stability is assured. Empiric antibiotic treatment is administered for several days and anticoagulation treatment is given until discharge. All patients are prescribed aspirin and clopidogrel for several months.

- **Transapical approach:** This approach requires a team consisting of cardiac surgeons and interventional cardiologists [17,18]. No vascular catheterization is performed. After a left anterolateral intercostal incision is made to expose the cardiac apex, the delivery system is inserted into the left ventricular cavity and the valve is implanted [Figure 2B]. This approach is more invasive than the other two and is performed under general anesthesia. Therefore, those patients who are not candidates for valve replacement may not be considered for transapical PAVI either. Nonetheless, the transapical approach has several important advantages. First, there is no delivery of the system via the peripheral vessels, the ascending aorta, or cardiac chambers, with the attendant risks. Second, unlike conventional valve replacement, there is no need for cardiopulmonary bypass or manipulation in the ascending aorta, potentially decreasing the risk of periprocedural stroke. In a report of their experience with this method in 59 patients with severe co-morbidity (Logistic euroSCORE 27%), Walther et al. [19] reported that transapical implantation success was 90%, there were no major procedural failures and excellent hemodynamics in most cases after several months of follow-up. There were no procedure-related deaths or stroke; however, in-hospital mortality

Preliminary studies show that this procedure is both feasible and effective in elderly patients with aortic stenosis in the short and medium term

PAVI = percutaneous aortic valve implantation

was 13.6%. During the last year, this approach was used in several centers worldwide.

TYPES OF VALVES AND CLINICAL STUDIES

Early implants were performed using the Cribier-Edwards valve (Edwards Lifesciences, Irvine, CA, USA), which are composed of three leaflets of animal pericardium sutured to a balloon-inflated stent 23 mm or 26 mm in diameter [Figure 3A]. The valves are designed to a length of 14 mm to avoid disturbing the coronary vessel ostium or the anterior leaflet of the mitral valve during delivery. The "RetroFlex" tip deflectable catheter with the "Nose Cone" security feature allows for better control of the delivery system as well as centralization of the device while passing retrograde though the aorta towards implantation within the calcified (pre-dilated) native valve. Cribier et al. [20] described the first 27 patients treated by PAVI with the Edwards valve, 23 with the antegrade approach and 4 with the retrograde approach. All were elders, with severe co-morbidities and ineligible for conventional therapy ("no-option" patients). After the procedure, mean valve area increased to 1.7 cm^2, yielding a small but significant improvement in global function of the left ventricle. Importantly, there were no deaths directly related to the procedure.

More recently, Webb et al. [21] reported the outcome of the first 50 severe symptomatic aortic stenosis patients treated with the Edwards valve implant in Vancouver, Canada, all with the retrograde approach. Mean patient age was 82 years. In all cases, at least two physicians agreed that valve replacement was contraindicated because of high surgical risk. PAVI was successful in 86% of patients. In some cases where the valve was incorrectly positioned it was delivered distally to the aortic arc or to the descending aorta where it was left without any disturbance. After the procedure, a small but significant increase in left ventricular ejection fraction was documented, in addition to an increase in mean valve area to 1.7 cm^2 [Figure 4]. On long-term follow-up of 1 year, and sometimes even 2 years, there was not a single case of valve restenosis or malfunction. The mortality rate was 12% in the first month after the procedure, which was lower than the 28% predicted mortality according to the patients' preprocedural euroSCOREs. Nevertheless, it is important to emphasize that the accuracy of the algorithms predicting mortality risk after aortic valve replacement remains controversial [22].

Another important finding in the study of Webb et al. was the difference in procedural success (76% vs. 96%) and 1 month mortality (16% vs. 8%) between patients treated at the beginning of the learning curve and those treated later, indicating the importance of physician experience [21]. These results might have been affected by patient selection bias, which is also experience-related. To date, more than 1500 patients have been treated with the percutaneous aortic valve replacement technique and the Cribier-Edwards valve, which was slightly modified and is now called the Edwards-Sapien valve.

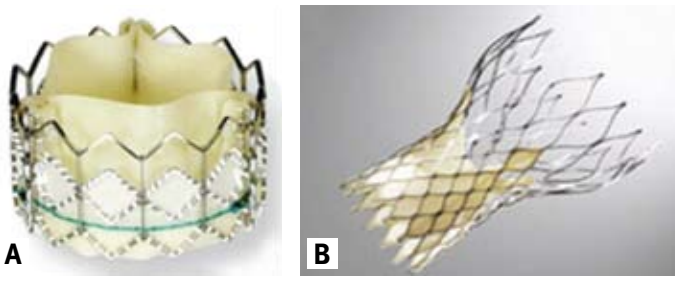

Figure 3. [A] The Edwards stent mounted prosthesis. An equine pericardial valve is sewn within a stainless steel frame. A fabric skirt covers the bottom third of the stent. **[B]** The CoreValve device. A self-expanding Nitinol frame within which is mounted a trileaflet tissue valve.

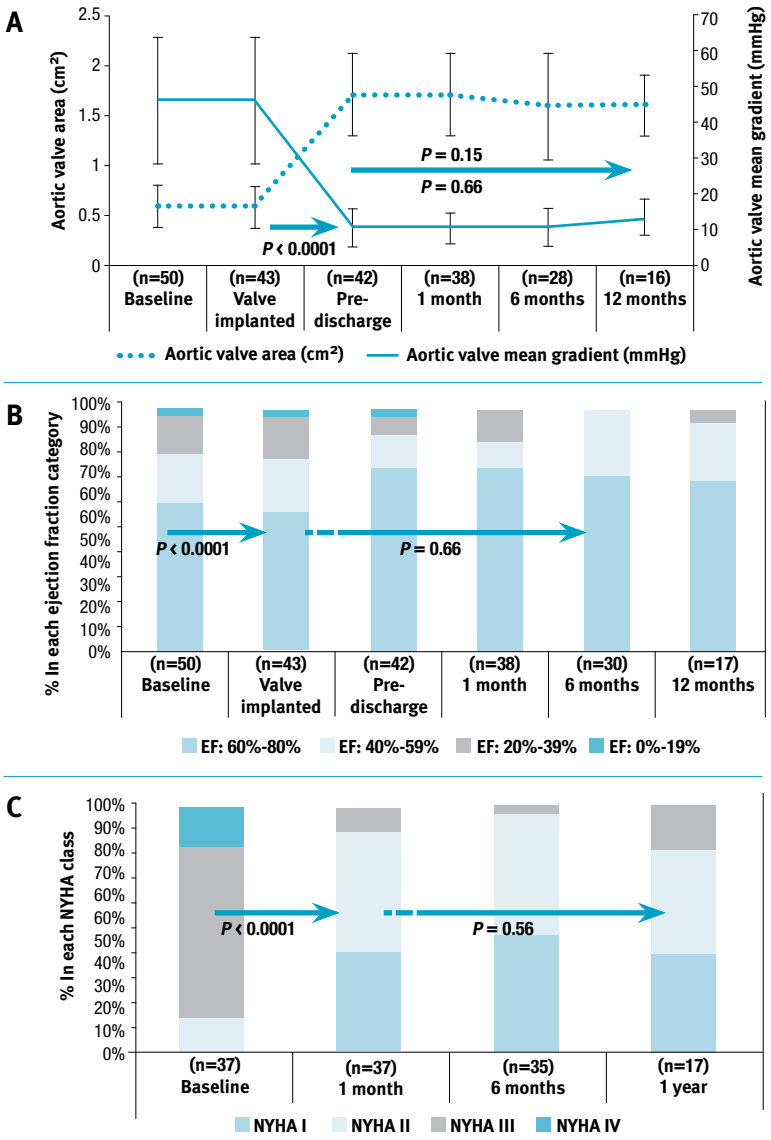

Figure 4. Clinical results of the first group of patients treated by Webb et al. [21]. After the procedure there was **[A]** a significant improvement in aortic valve area and pressure gradient, **[B]** left ventricle ejection fraction, and **[C]** heart failure severity. These results were maintained during 1 year of follow-up.

The CoreValve system (CoreValve Inc. Irvine, CA, USA), also called ReValving technology, is composed of a valve encircled by a 45 mm long cage [Figure 3B]. It was initially intended for use by the retrograde approach only. The valve has a unique, three-segment configuration: the lower segment exerts pressure directly on left ventricular outflow and the native valve and compresses its leaflets; the middle segment includes the implanted valve, which is made of animal pericardium, and protects the flow in the direction of the coronary vessels so that coronary angiography, if necessary, can still be performed after implantation; the long upper segment is wider and attached to the ascending aorta, providing longitudinal stability to the total system. In contrast to the balloon-expandable Edwards system, the CoreValve is self-expandable for intended increased durability, although balloon expansion during use is not uncommon [23]. The possibility to expand the system after implantation decreases the risk of perivalvular leak. Because of this feature, the system could be extendable to patients who underwent surgical biologic valve replacement ("valve in valve" procedure) [24]. Were physicians able to effectively perform PAVI inside a degenerative implanted biologic valve, the use of biologic valves for aortic valve replacement would likely increase because valve malfunction can be treated without the need for redo surgery. The CoreValve system was first applied in humans by Grube et al. in 2005 [25]. Early reports of procedure-related complications and a higher than predicted mortality rate were followed by a series of technical modifications to decrease the size of the catheter for safer delivery through the peripheral arteries. The current (third-generation) model is significantly improved and has a diameter of only 18 Fr. The implantation results of the second- and third-generation systems in 86 patients in several centers in Germany and Canada have recently been published [23]. Most patients were women, selected because of the small size of the implanted valve. Their mean age was 82 years and they had a high mean euroSCORE of 21.7%. The procedural success rate was 88%. There was a dramatic improvement in hemodynamic parameters, including an increase in valve area to 1.7 cm^2. Valve regurgitation worsened in only a minority of cases. In the first month after the procedure the mortality rate was 12%; half of these deaths occurred in the first 2 days. Tamponade occurred in 10% of patients in the first month after the procedure and was the cause of death in some cases, while stroke occurred in 10%. Furthermore, urgent cardiac surgery to release the device was necessary in 6% of patients. At the time of writing the present review, more than 1500 patients had been treated with the CoreValve stent. According to still-unpublished results, the procedural success rate for the 18 Fr device is 92%, with only 4% of patients requiring aortic valve replacement in the first post-procedural month.

SUMMARY AND FUTURE PERSPECTIVES

Recent decades have witnessed a clear trend toward a lower level of invasiveness in medical procedures in general and cardiac procedures in particular. Cardiac catheterization currently provides a major alternative to surgery for the treatment of mitral valve stenosis [26,27], and efforts are being directed towards developing a percutaneous option for mitral valve regurgitation and pulmonary valve disease as well [28-31]. Though still in its early stages, and not yet sufficiently viable to replace conventional methods in low risk patients, percutaneous treatment of aortic stenosis holds promise for providing symptomatic relief and probably longevity for patients who are ineligible for surgery. Preliminary studies show that PAVI is both feasible and effective in elderly patients with aortic stenosis in the short and medium term. In contrast to balloon valvuloplasty, the hemodynamic improvement after valve implantation is dramatic and stable. At the same time, although the initial clinical studies were performed in patients with severe co-morbidity, we need to consider the significant adverse effects of PAVI and the 10–15% early mortality rate. The experience of the surgeon seems to be a crucial determining factor.

In contrast to balloon valvuloplasty, the hemodynamic improvement after valve implantation is dramatic and stable

At present, we do not have significant scientific proof that percutaneous therapy is superior to surgery, not even in patients at high risk. Comparisons of PAVI mortality rates and predicted mortality risk after surgery are not sufficient, and clinicians are awaiting the results of two ongoing large randomized multicenter trials, the PARTNER-US and the PARTNER-EU, that evaluate PAVI against aortic valve replacement and medical therapy.

Achieving optimal results with this novel technique requires the collaboration of a multidisciplinary team of experts in echocardiography, intensive care, vascular surgery, radiology, cardiothoracic surgery and invasive cardiology. The contribution of cardiovascular imaging to percutaneous valve therapy cannot be underestimated. Using computed tomography angiography, physicians can accurately quantify and vividly display the peripheral vasculature and predict the risk using the retrograde approach. Magnetic resonance imaging of the aortic valve and ascending aorta allows physicians to better plan procedures and identify patients at risk of a disturbance to the coronary circulation, such as those with bulky leaflets.

We expect that in the future, with continuous improvement in patient selection, technology and technique, we may see a substantial increase in application of the percutaneous treatment in valvular diseases in general and in aortic stenosis specifically. By the time of this writing, around 3000 PAVI procedures had been performed worldwide. There are currently more than 12 different kinds of valves available for this use.

In Israel, both PAVI devices were approved by the Ministry of Health (i.e., Device Section Authorization) for clinical use and commercial distribution. However, since the procedure has not been included in the "Health Basket," there is no reimbursement code yet for PAVI and the medical providers (health management organizations) are not obliged to pay for the costly service. Therefore, in the meantime, Israeli medical institutions must make their estimates regarding the potential clinical utilities and merits of implementing the procedure and weigh it against the projected costs associated with the device. Those calculations should take into account not only the financial issues but also the overwhelming sickness of those patients and lack of alternative acceptable therapeutic options. In Israel, there are about 1000 isolated aortic valve replacement surgeries per year. Assuming the 10–20% non-surgical and/or poor candidates for surgery we should expect that 100–200 patients will be candidates for PAVI procedures per year according to the current highly restricted indications. As of early 2009, 35 PAVI procedures have been performed in Israel (23 using CoreValve system and 12 using Edwards valves). Procedural details will be reported by the operating sites during the upcoming Israel Heart Society national meeting.

Correspondence:
Dr. R. Kornowski
Dept. of Cardiology, Rabin Medical Center, Petah Tikva 49100, Israel
Phone: (972-3) 937-6441
Fax: (972-3) 923-1016
email: rkornowski@clalit.org.il

References

1. Nkomo VT, Gardin JM, Skelton TN, et al. Burden of valvular heart diseases: a population-based study. *Lancet* 2006; 368(9540): 1005-11.
2. Vahanian A, Baumgartner H, Bax J, et al. Guidelines on the management of valvular heart disease. *Eur Heart J* 2007; 28(2): 230-68.
3. Iung B, Cachier A, Baron G, et al. Decision-making in elderly patients with severe aortic stenosis: why are so many denied surgery? *Eur Heart J* 2005; 26(24): 2714-20.
4. Varadarajan P, Kapoor N, Bansal RC, et al. Clinical profile and natural history of 453 nonsurgically managed patients with severe aortic stenosis. *Ann Thorac Surg* 2006; 82(6): 2111-15.
5. Otto CM, Mickel MC, Kennedy JW, et al. Three-year outcome after balloon aortic valvuloplasty. Insights into prognosis of valvular aortic stenosis. *Circulation* 1994; 89(2): 642-50.
6. Feldman T, Glagov S, Carroll JD. Restenosis following successful balloon valvuloplasty: bone formation in aortic valve leaflets. *Cathet Cardiovasc Diagn* 1993; 29(1): 1-7.
7. Klein A, Lee K, Gera A, et al. Long-term mortality, cause of death, and temporal trends in complications after percutaneous aortic balloon valvuloplasty for calcific aortic stenosis. *J Interv Cardiol* 2006; 19(3): 269-75.
8. Cribier A, Eltchaninoff H, Bash A, et al. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. *Circulation* 2002; 106: 3006-8.
9. Cribier A, Savin T, Saoudi N, et al. Percutaneous transluminal valvuloplasty of acquired aortic stenosis in elderly patients: an alternative to valve replacement? *Lancet* 1986; 1: 63-7.
10. O'Neill WW. Predictors of long-term survival after percutaneous aortic valvuloplasty: report of the Mansfield Scientific Balloon Aortic Valvuloplasty Registry. *J Am Coll Cardiol* 1991; 17(1): 193-8.
11. Bonow RO, Carabello BA, Kanu C, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1998 Guidelines for the Management of Patients with Valvular Heart Disease). *Circulation* 2006; 114: e84-231.
12. Andersen HR, Knudsen LL, Hasenkam JM. Transluminal implantation of artificial heart valves. Description of new expandable aortic valve and initial results with implantation by catheter technique in closed chest pigs. *Eur Heart J* 1992; 13: 704-8.
13. Bonhoeffer P, Boudjemline Y, Saliba Z, et al. Percutaneous replacement of pulmonary valve in a right-ventricle to pulmonary-artery prosthetic conduit with valve dysfunction. *Lancet* 2000; 356: 1403-5.
14. Bauer F, Eltchaninoff H, Tron C, et al. Acute improvement in global and regional left ventricular systolic function after percutaneous heart valve implantation in patients with symptomatic aortic stenosis. *Circulation* 2004; 110: 1473-6.
15. Cribier A, Eltchaninoff H, Tron C, et al. Early experience with percutaneous transcatheter implantation of heart valve prosthesis for the treatment of end-stage inoperable patients with calcific aortic stenosis. *J Am Coll Cardiol* 2004; 43: 698-703.
16. Webb JG, Chandavimol M, Thompson CR, et al. Percutaneous aortic valve implantation retrograde from the femoral artery. *Circulation* 2006; 113: 842-50.
17. Dewey TM, Walther T, Doss M, et al. Transapical aortic valve implantation: an animal feasibility study. *Ann Thorac Surg* 2006; 82(1): 110-16.
18. Lichtenstein SV, Cheung A, Ye J, et al. Transapical transcatheter aortic valve implantation in humans: initial clinical experience. *Circulation* 2006; 114: 591-6.
19. Walther T, Simon P, Dewey T, et al. Transapical minimally invasive aortic valve implantation multicenter experience. *Circulation* 2007; 116[Suppl I]: I-240-5.
20. Cribier A, Eltchaninoff H, Tron C, et al. Treatment of calcific aortic stenosis with the percutaneous heart valve mid-term follow-up from the initial feasibility studies: the French Experience. *J Am Coll Cardiol* 2006; 47: 1214-23.
21. Webb JG, Pasupati S, Humphries K, et al. Percutaneous transarterial aortic valve replacement in selected high-risk patients with aortic stenosis. *Circulation* 2007; 116: 755-63.
22. Youn YN, Kwak YL, Yoo KJ. Can the EuroSCORE predict the early and mid-term mortality after off-pump coronary artery bypass grafting? *Ann Thorac Surg* 2007; 83(6): 2111-17.
23. Grube E, Schuler G, Buellesfeld L, et al. Percutaneous aortic valve replacement for severe aortic stenosis in high-risk patients using the second- and current third- generation self-expanding CoreValve prosthesis device: success and 30-day clinical outcome. *J Am Coll Cardiol* 2007; 50: 69-76.
24. Wenaweser P, Buellesfeld L, Gerckens U, et al. Percutaneous aortic valve replacement for severe aortic regurgitation in degenerated bioprosthesis: the first valve in valve procedure using the Corevalve revalving system. *Catheter Cardiovasc Interv* 2007; 70(5): 760-4.
25. Grube E, Laborde JC, Gerckens U, et al. Percutaneous implantation of the CoreValve self-expanding valve prosthesis in high risk patients with aortic valve disease: the Siegburg first-in-man study. *Circulation* 2006; 114: 1616-24.
26. Carroll JD, Feldman T. Percutaneous mitral balloon valvotomy and the new demographics of mitral stenosis. *JAMA* 1993; 270: 1731-6.
27. Palacios IF, Sanchez PL, Harrell LC, et al. Which patients benefit from percutaneous mitral balloon valvuloplasty? Pre-valvuloplasty and postvalvuloplasty variables that predict long-term outcome. *Circulation* 2002; 105: 1465-71.
28. Maniu CV, Patel JB, Reuter DG, et al. Acute and chronic reduction of functional mitral regurgitation in experimental heart failure by percutaneous mitral annuloplasty. *J Am Coll Cardiol* 2004; 44: 1652-61.
29. Webb JG, Harnek J, Munt BI, et al. Percutaneous transvenous mitral annuloplasty: initial human experience with device implantation in the coronary sinus. *Circulation* 2006; 113: 851-5.
30. Feldman T, Wasserman HS, Herrmann HC, et al. Percutaneous mitral valve repair using the edge-to-edge technique: six-month results of the EVEREST phase I clinical trial. *J Am Coll Cardiol* 2005; 46: 2134-40.
31. Lurz P, Coats L, Khambadkone S, et al. Percutaneous pulmonary valve implantation: impact of evolving technology and learning curve on clinical outcome. *Circulation* 2008; 117(15): 1964-72.