Percutaneous Implantation of the Self-Expandable CoreValve for High Risk Patients with Severe Aortic Valve Stenosis: Early Israeli Experience

Haim Danenberg MD[1], Ariel Finkelstein MD[2], Ran Kornowski MD[3], Amit Segev MS[4], Danny Dvir MD[3], Dan Gilon MD[1], Gad Keren MD[2], Alex Sagie MD[3], Micha Feinberg MD[4], Ehud Schwammenthal MD[4], Shmuel Banai MD[2], Chaim Lotan MD[1] and Victor Guetta MD[4]

Departments of Cardiology at:
[1]Hadassah-Hebrew University Medical Center, Jerusalem, Israel
[2]Tel Aviv Sourasky Medical Center, Tel Aviv, Israel
[3]Rabin Medical Center (Beilinson Campus), Petah Tikva, Israel
[4]Sheba Medical Center, Tel Hashomer, Israel

ABSTRACT: **Background:** The prevalence of aortic stenosis increases with advancing age. Once symptoms occur the prognosis in patients with severe aortic stenosis is poor. The current and recommended treatment of choice for these patients is surgical aortic valve replacement. However, many patients, mainly the very elderly and those with major comorbidities, are considered to be at high surgical risk and are therefore denied treatment. Recently, a transcatheter alternative to surgical AVR has emerged.

Objectives: To describe the first year experience and 30 day outcome of transcatheter aortic self-expandable CoreValve implantation in Israel.

Methods: Transcatheter aortic valve implantation using the CoreValve system has been performed in Israel since September 2008. In the following year 55 patients underwent CoreValve TAVI in four Israeli centers.

Results: Patients' mean age was 81.7 ± 7.1 years; there were 35 females and 20 males. The mean valve area by echocardiogram was 0.63 ± 0.16 cm^2. The calculated mean logistic Euroscore was 19.3 ± 8%. Following TAVI, mean transvalvular gradient decreased from baseline levels of 51 ± 13 to 9 ± 3 mmHg. The rate of procedural success was 98%. One patient died on the first day post-procedure (1.8%) and all-cause 30 day mortality was 5.5% (3 of 55 patients). One patient had a significant post-procedural aortic regurgitation of › grade 2. Symptomatic improvement was evident in most patients, with reduction in functional capacity grade from 3.2 ± 0.6 at baseline to 1.4 ± 0.7. The most common post-procedural complication was complete heart block, which necessitated permanent pacemaker implantation in 37% of patients.

Conclusions: The Israeli first year experience of transcatheter aortic valve implantation using the CoreValve self-expandable system demonstrates an effective and safe procedure for the treatment of severe aortic stenosis in patients at high surgical risk.

IMAJ 2010; 12: 468–471

KEY WORDS: CoreValve, aortic stenosis, aortic replacement

For Editorial see page 503

Aortic valve stenosis is a common clinical syndrome in the elderly population. The natural course of symptomatic AS is grim and is associated with augmented short-term mortality and over 60% mortality in 5 years [1]. Surgical aortic valve replacement is the treatment of choice for severe symptomatic AS, ameliorating symptoms, improving left ventricular function and prolonging life. Unfortunately, a large number of AS patients are old and fragile and are thus declined surgery due to comorbidities and/or high surgical risk. The rate of such high risk and inoperable patients is reported as ranging between 30 and 50% [2-4]. Recently, a novel therapy for such patients was launched. In 2002 Alain Cribier performed the first transcatheter aortic valve implantation in a patient with critical AS who suffered from cardiogenic shock [5]. Since then, two TAVI systems were introduced for clinical use: the balloon-expandable Edwards Sapien™ valve (Edwards Life Sciences, USA) and the self-expandable CoreValve Revalving™ system (CoreValve – Medtronic, USA). Both systems are available for retrograde implantation via the femoral artery access and the Edwards valve is available for transapical antegrade implantation as well [for review see 6]. The clinical application of TAVI is rapidly expanding with over 5000 valves already implanted worldwide and the number is rapidly growing. In September 2008 the first transcatheter CoreValve implantation was performed in Israel, and 55 patients were treated with this

AVR = aortic valve replacement
TAVI = transcatheter aortic valve implantation
AS = aortic valve stenosis

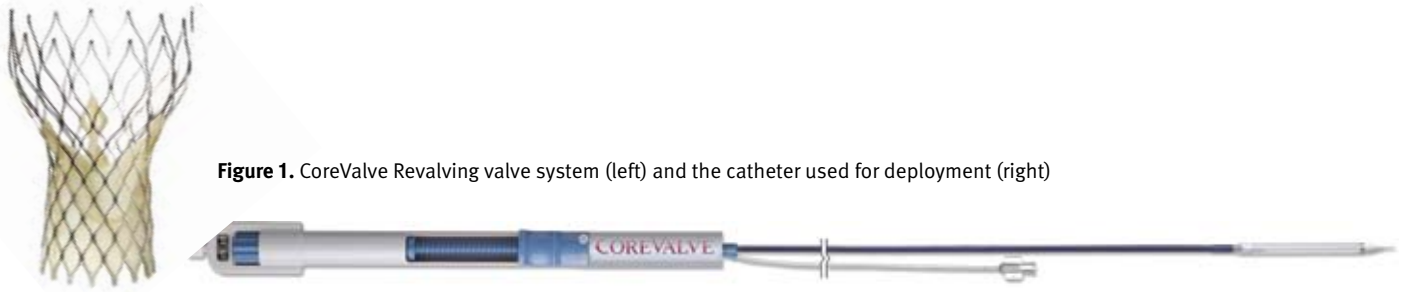


Figure 1. CoreValve Revalving valve system (left) and the catheter used for deployment (right)

system in the following year. This report describes the initial Israeli experience with this new technique.

PATIENTS AND METHODS

DEVICE AND PROCEDURAL DESCRIPTION

The CoreValve Revalving system is a tri-leaflet porcine pericardial tissue mounted on a self-expanding multilevel nitinol frame, which extends from the left ventricular outflow tract into the aortic root [Figure 1]. The shape-memory capacity of nitinol allows crimping into a low profile 18F loading system and expansion to its full predesigned form upon implantation. The frame contains three levels that differ in radial and hoop strength, allowing appropriate orientation, anchoring and valve placement without mitigating coronary flow. The prosthesis is sized according to the aortic annular diameter and has the advantage of being self-centered and partially repositionable during deployment. Currently, the CoreValve system is available in sizes of 26 and 29 mm inflow diameter which fit an annular diameter of 20–27 mm. Prosthesis size selection is based on the measurements of the aortic valvular complex dimensions that are obtained by echo, angiography and in certain cases computed tomography or magnetic resonance imaging. The procedure is performed in the catheterization laboratory under systemic or local anesthesia according to the patient's condition and the operator's discretion. Most cases are performed percutaneously via a transfemoral approach, although surgical exposure of the access site should be performed in selective cases. In cases in which the femoral approach is precluded, implantation may be performed via the subclavian artery. Prior to implantation, the calcific native valve is dilated with a balloon under rapid ventricular pacing performed using a temporary pacemaker. The prosthesis is then deployed in a controlled manner under fluoroscopic guidance [Figure 2]. The arteriotomy is closed percutaneously with a large-bore (10F) arterial closure device (Perclose Prostar XL™, Abbott Vascular, USA). The first 12–14 cases in each center were performed under the supervision of a clinical proctor. Premedication includes low dose aspirin (75–325 mg/day) and copidogrel (75 mg/day), which are to be continued for a minimum of 6 months following valve implantation.

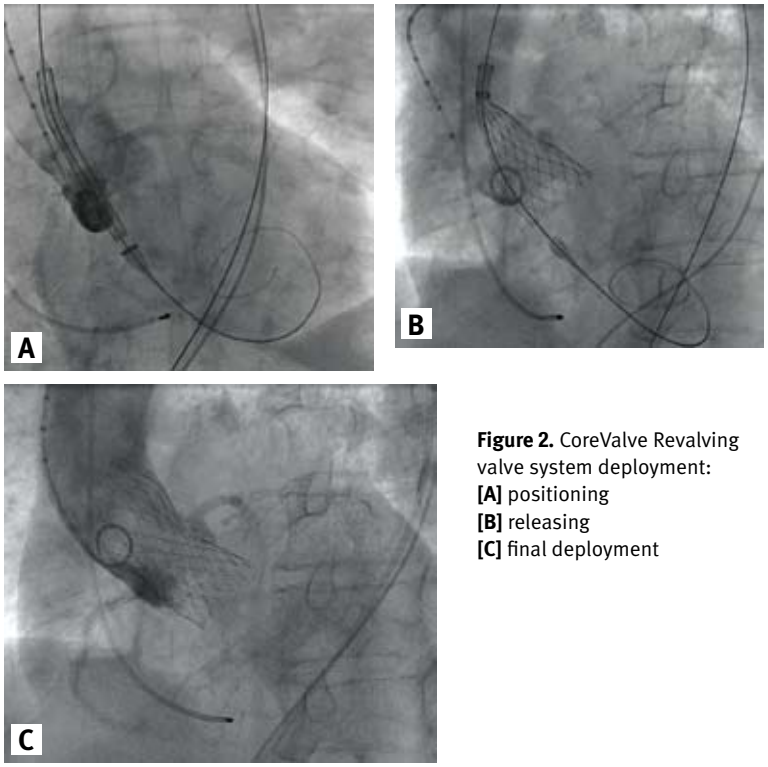


Figure 2. CoreValve Revalving valve system deployment:
[A] positioning
[B] releasing
[C] final deployment

PATIENTS

Between September 2008 and September 2009, 55 patients underwent CoreValve TAVI at four Israeli medical centers. Patients underwent evaluation by a cardiovascular team that consisted of cardiologists and cardiothoracic surgeons. A consensus was reached for excessive high surgical risk or an inoperable state. The potential risks and medical benefits were explained and all patients provided a written consent. In September 2008 the first CoreValve implantation was performed in Israel in an 80 year old woman with severe symptomatic AS and multiple comorbidities including severe pulmonary disease that amended her high surgical risk. A joint ongoing prospective registry is conducted by the medical centers that perform CoreValve TAVI and record the clinical, echocardiographic and angiographic data at baseline and follow-up.

STATISTICAL ANALYSIS

Continuous variables are presented as means ± standard deviations. Categorical variables are presented as frequencies in percentage of total cohort. Significance was calculated using the paired Student *t*-test. $P < 0.05$ was considered statistically significant.

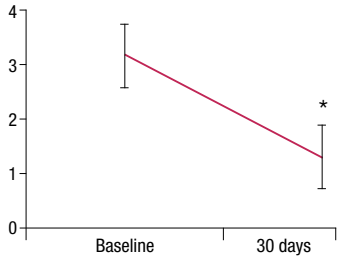
Table 1. Demographic and baseline characteristics of patients undergoing TAVI

	Mean ± SD/ % (N=55)
Age (yrs)	81.5 ± 7.1
Logistic EuroSCORE (%)	19.3 ± 8.1
Female	64%
NYHA	I-II: 5.5% III-IV: 94.5%
Aortic valve area (cm²)	0.63 ± 0.16
Peak gradient (mmHg)	85 ± 23
Mean gradient (mmHg)	51 ± 13
Peak to peak gradient (mmHg)	76 ± 21
Left ventricular ejection fraction (%)	58 ± 7

Table 2. Adverse events 30 days post-TAVI

	%
Death	5.5
Aortic dissection	0
Cardiac tamponade	5.5
Cardiac perforation	0
Access site complications	16
Major bleeding	3.6
Conversion to surgery	0
Myocardial infarction	0
Pacemaker	37
Renal failure	3.6
Stroke	0
Transient ischemic attack	1.8

Figure 3. NYHA functional capacity (mean ± SD) at baseline and 30 days after TAVI



* $P < 0.05$

RESULTS

Baseline clinical and echocardiographic characteristics of the registry cohort are shown in Table 1. Of note is the relatively advanced age of the treated patients. Mean age was 81.7 ± 7.1 years. Mean valve area was estimated by echo as 0.63 ± 0.16 cm² with a maximal gradient of 85 ± 23 mmHg and a mean gradient of 51 ± 13 mmHg. Patients were symptomatic prior to intervention, with mean New York Heart Association functional capacity 3.2 ± 0.6. The high surgical risk that precluded surgery was estimated as a logistic Euroscore of 19.3 ± 8 (range 6–49). Common comorbidities included ischemic heart disease in 43.6% of the patients and chronic lung disease in 40%; 23.6% of the patients had previous chest surgery and in 17% a "porcelain" highly calcified aorta was recorded by CT scan.

Fifty-two procedures were performed via the femoral artery and in 3 cases TAVI was performed via the subclavian artery since femoral anatomy precluded the femoral approach. Fifty-three procedures were performed under general anesthesia and 2 under mild sedation. Continuous transesophageal echocardiography throughout the procedure was performed in 44 cases. Immediate hemodynamic improvement was achieved in all patients. Peak to peak gradient was significantly reduced and maximal echocardiographic gradient was 16.2 ± 5.5 immediately following valve implantation. In two patients severe aortic regurgitation was observed and was treated with further balloon dilatation. In one case the device dislodged and was successfully retrieved and properly repositioned. Nine patients (16.3%) suffered vascular complications, including strictures and perforations, at the end of the procedure. In most cases these were successfully treated percutaneously. Procedural mortality occurred in one patient with a vascular complication due to iliac perforation and massive retroperitoneal bleeding.

All-cause mortality rate at 30 days (including procedural mortality) was 5.5% (3 of 55 patients). Another two deaths occurred: one patient died on day 2 following TAVI due to pericardial tamponade and the other died 2 weeks following TAVI due to hemorrhagic stroke. Cumulative adverse events at 30 days are presented in Table 2. Complete heart block that warranted permanent pacemaker implantation occurred in 19 of 51 patients (37%, four patients had previous pacemaker implantation and are thus precluded from the analysis). One patient had residual aortic regurgitation, grade III. Mean hospital stay was 8.8 ± 6 days. Symptomatic relief was successfully achieved in most of our patients. Mean NYHA functional capacity decreased from a baseline level of 3.2 ± 0.6 to 1.3 ± 0.6 after 30 days [Figure 3].

NYHA = New York Heart Association

DISCUSSION

Transcatheter aortic valve implantation is a novel technique for the treatment of patients who are currently refused surgery because of the anticipated high surgical risk. The procedure, first performed in 2002, has since gained popularity and is used worldwide. Two stent-based valves are currently available for use, although they differ in dimensions, deployment strategy and complications. TAVI calls for a multidisciplinary effort and intensive education and training of the operating teams. The screening process is complex and involves both cardiologists and surgeons. The procedure and the post-procedural follow-up require acquisition of new skills that were until recently out of the domain of the interventional cardiologists.

The results of this first-year Israeli cohort indicate that the CoreValve-based TAVI with the self-expandable system is a viable, effective and relatively safe therapeutic technique for patients who until recently were refused any therapy. Feasibility and safety were proven by the high procedural success rate and relatively low 30 day mortality for very high risk patients (5.5%). Major symptomatic improvement was achieved in the vast majority of patients and the procedure was found effective in reducing atrioventricular gradients and alleviating patients' symptoms. Similar to the acquisition of any new technique, TAVI is not free from 'learning curve' hurdles. We strongly believe that expanding experience alongside technical advances of the TAVI system will result in further improvements in clinical outcome.

The mortality rate at 30 days in our series compares or is even somewhat lower than that reported in other series using the CoreValve Revalving system [7-9] or the Edwards-Sapien device [6,10,11]. However, comparison of these series is difficult due to differences in case selection and patient characteristics.

The most prevalent complication in our series was high degree and/or complete heart block that warranted implantation of a permanent pacemaker in 37% of our cohort. The reason for this block is probably due to the position of the prosthesis and the pressure applied on the left ventricular outflow conduction system. Certain baseline characteristics correlate with post-procedural need for pacemaker and include left bundle branch block, left axis deviation, and the thickness of the non-coronary cusp [12]. Further studies are needed to accurately identify patients at risk as well as procedural parameters that lead to conduction disturbances. Preemptive pacemaker implantation should be considered prior to TAVI in a subgroup of patients defined as being at high risk for significant conduction disturbances.

In conclusion, the initial Israeli experience with the CoreValve TAVI system for severe atrial stenosis is encouraging, proving the usefulness of this technique to treat a large number of patients who until recently were left untreated. Further attempts should be made to improve the procedure and reduce procedural and peri-procedural mortality and complication rates. Despite the favorable data, we believe that at present the procedure should be limited to high risk and inoperable AS patients and that uncontrolled expansion of TAVI indications should be avoided. Future studies and increasing experience will determine the future of this revolutionary technique and the extent to which TAVI indications can be expanded.

Corresponding author:
Dr. V. Guetta
Director, Cardiac Catheterization Service and Deputy Director, Heart Institute, Sheba Medical Center, Tel Hashomer 52621, Israel
Phone: (972-3) 530-5273
Fax: (972-3) 530-5789
email: guettav@gmail.com

References

1. Varadarajan P, Kapoor N, Bansal RC, Pai RG. Clinical profile and natural history of 453 nonsurgically managed patients with severe aortic stenosis. *Ann Thorac Surg* 2006; 82(6): 2111-15.
2. Charlson E, Legedza AT, Hamel MB. Decision-making and outcomes in severe symptomatic aortic stenosis. *J Heart Valve Dis* 2006; 15(3): 312-21.
3. Iung B, Baron G, Butchart EG, et al. A prospective survey of patients with valvular heart disease in Europe: the Euro Heart Survey on Valvular Heart Disease. *Eur Heart J* 2003; 24(13): 1231-43.
4. Pellikka PA, Sarano ME, Nishimura RA, et al. Outcome of 622 adults with asymptomatic, hemodynamically significant aortic stenosis during prolonged follow-up. *Circulation* 2005; 111(24): 3290-5.
5. 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(24): 3006-8.
6. Zajarias A, Cribier AG. Outcomes and safety of percutaneous aortic valve replacement. *J Am Coll Cardiol* 2009; 53(20): 1829-36.
7. 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(1): 69-76.
8. Laborde J. Transcatheter aortic valve implantation with the CoreValve Revalving system. Presented at the 2008 TCT meeting, Washington DC, USA.
9. Piazza N, Grube E, Gerckens U, et al. Procedural and 30-day outcomes following transcatheter aortic valve implantation using the third generation (18 Fr) corevalve revalving system: results from the multicentre, expanded evaluation registry 1-year following CE mark approval. *Eurointervention* 2008; 4(2): 242-9.
10. Walther T, Falk V, Kempfert J, et al. Transapical minimally invasive aortic valve implantation; the initial 50 patients. *Eur J Cardiothorac Surg* 2008; 33(6): 983-8.
11. Webb JG, Altwegg L, Boone RH, et al. Transcatheter aortic valve implantation: impact on clinical and valve-related outcomes. *Circulation* 2009; 119(23): 3009-16.
12. Jilaihawi H, Chin D, Vasa-Nicotera M, et al. Predictors for permanent pacemaker requirement after transcatheter aortic valve implantation with the CoreValve bioprosthesis. *Am Heart J* 2009; 157(5): 860-6.

"Once we assuage our conscience by calling something a "necessary evil," it begins to look more and more necessary and less and less evil"

Sydney J. Harris (1917-1986), American journalist