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Institutional report - Valves

Procedural, 30-day and one year outcome following CoreValve or Edwards transcatheter aortic valve implantation: results of the Belgian national registry☆

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Abstract

We report clinical outcomes following transcatheter aortic valve implantation (TAVI), using the CoreValve revalving system (18 Fr transfemoral or subclavian) or the Edwards Sapien valve (22 Fr transfemoral or 24 Fr transapical) as part of a Belgian prospective non-randomized multicentre registry. All 15 Belgian centres performing TAVI participated to this registry (seven exclusively Edwards Sapien, eight exclusively CoreValve). All consecutive high-risk symptomatic patients with severe aortic stenosis were evaluated by a heart team and screened for eligibility for TAVI. Three hundred and twenty-eight patients underwent TAVI with CoreValve ($n=141$; eight subclavian and 133 transfemoral) or Edwards Sapien ($n=187$; 99 transfemoral and 88 transapical) up to April 2010. Procedural success was 97%. One-month survival was 88% for the Edwards and 89% for the CoreValve treated patients. One-month mortality was both related to cardiac and non-cardiac reasons. Overall one-year survival was 78% in the CoreValve transfemoral treated patients, 100% in the CoreValve subclavian treated patients, 82% in the Edwards transfemoral treated patients and 63% in the Edwards transapical treated patients. This mid-term mortality was mainly related to age-related, non-cardiac complications.

Keywords: Aortic stenosis; Transcatheter aortic valve implantation; Registry

1. Introduction

Surgical aortic valve replacement (SAVR) is the primary treatment modality recommended for severe aortic stenosis, offering both symptomatic and prognostic benefits. However, the need for a less-invasive, non-surgical treatment option for high-risk patients has recently culminated in development of transcatheter aortic valve implantation (TAVI). Currently, two devices are clinically in use. The Edwards Sapien valve is a bovine pericardium prosthesis mounted on a balloon-expandable stent that is placed in the subcoronary position. It can be placed by an antegrade (transapical) or retrograde (transfemoral) approach. The CoreValve transcatheter aortic valve is a self-expanding nitinol frame porcine pericardium prosthesis, placed by a retrograde (transfemoral or subclavian) approach.

Randomized trials that are currently underway will confirm procedural safety and guide the applicability of this technology. In the mean time, carefully performed national registries monitoring all TAVI outcome data of both devices can already be of value in defining the potential clinical role of this new technology in high-risk symptomatic patients refused for SAVR [1–4]. The Belgian TAVI Registry is a prospective, non-randomized multicenter national registry, aiming to include and follow-up all consecutive Belgian TAVI procedures.

2. Methods

2.1. The Belgian TAVI Registry

All 15 Belgian cardiac centres, performing TAVI, participated to this Belgian TAVI Registry. In seven of these centres, the Edwards Sapien valve was exclusively used and in eight of these, the CoreValve device was exclusively used. All consecutive TAVI procedures were included. Patient follow-up was obtained during and immediately after valve implantation, and at 1, 6 and 12 months.

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Table 1. Patient characteristics

	Edwards Sapien ($n=187$)	CoreValve ($n=141$)	Total population ($n=328$)	P-value
Age (years)	83±6	82±6	83±6	0.17
Gender (♂, %)	47	44	46	0.60
NYHA III, IV (%)	80	78	79	0.085
AVA (cm²)	0.59±0.15	0.63±0.13	0.61±0.15	0.073
Mean grad (mmHg)	48±16	49±16	49±16	0.67
LVEF (%)	52±15	59±13	55±14	0.000
Log EuroSCORE (%)	30±16	25±15	28±16	0.003
Atrial fibrillation (%)	32	27	30	0.33
Carotid disease (%)	27	10	20	0.000
CAD (%)	59	57	58	0.78
Porcelain aorta (%)	7	9	8	0.51
PVD (%)	38	18	29	0.000
Diabetes (%)	29	25	27	0.43
Pulm hypertension (%)	53	41	48	0.029
Mediastinal radiation (%)	4	6	5	0.48
COPD (%)	32	22	28	0.039
Renal failure (%)	22	18	20	0.41
Previous stroke/TIA (%)	20	9	15	0.006
Previous PM (%)	13	14	13	0.81
Previous CABG (%)	25	29	26	0.33
Previous valve surgery (%)	3	2	3	0.73

AVA, aortic valve area; LVEF, left ventricular ejection fraction; CAD, coronary artery disease; PVD, peripheral vascular disease; COPD, chronic obstructive pulmonary disease; TIA, transient ischemic attack; PM, pacemaker; CABG, coronary artery bypass grafting; NYHA, New York Heart Association.

Collection of patient data for the Belgian TAVI Registry was approved by the institutional Ethics Committee of the different participating centres.

Events and values collected are site recorded, and there are no core laboratories. Data pooling and statistical analysis was performed at the University of Antwerp.

2.2. Patients

TAVI was considered by the heart team in symptomatic patients with significant aortic valve stenosis who were not good candidates for surgical aortic valve replacement.

2.3. Statistical analysis

Continuous variables are presented as means (±S.D.) and were compared with the use of Student's t-test. In case of non-normal distribution, Mann–Whitney test was used. Categorical variables were compared with the use of Fisher's exact test. Survival curves for time-to-event variables were constructed on the basis of all available follow-up data with the use of Kaplan–Meier estimates and were compared with the use of the log-rank test.

3. Results

3.1. Patient population

Three hundred and twenty-eight consecutive patients who underwent TAVI until April 2010 were enrolled in this registry. Of the 187 Edwards treated patients, 53% ($n=99$) was treated transfemoral and 47% ($n=88$) by transapical approach. Of the 141 CoreValve treated patients, 94% ($n=133$) was treated transfemoral, and 6% ($n=8$) by subclavian approach. Baseline characteristics of the patients are reported in Table 1.

3.2. Procedural results and one-month clinical events and survival

Procedural success (Table 2) was very high in both treatment groups [Edwards (97%); CoreValve (98%); non-significant (NS)]. Procedural mortality was 3% in the Edwards treated patients and 2% in the CoreValve treated patients (non-significant, NS). Reasons of procedural mortality are summarized in Table 3. One month outcome data are summarized in Table 4.

Table 2. Procedural characteristics and outcome

n (%)	Edwards Sapien ($n=187$)	CoreValve ($n=141$)	Total population ($n=328$)	P-value
Access TF	99 (53)	133 (94)	232 (71)	0.000
Access TA	88 (47)	0 (0)	88 (27)	0.000
Access SC	0 (0)	8 (6)	8 (2)	0.000
Frame size				
23 mm	73 (39)			
26 mm	114 (61)	56 (40)		
29 mm		85 (60)		
Valve migration	5 (3)	4 (3)	9 (3)	1.00
Valve-in-valve	1 (0.5)	3 (2)	4 (1)	085
Procedural success	181 (97)	138 (98)	319 (97)	0.73
Procedural mortality	6 (3)	3 (2)	9 (3)	0.73

TF, transfemoral; TA, transapical; SC, subclavian.

Table 3. Causes of procedural mortality

LV perforation ($n=3$)
Edwards: 2
CoreValve: 1
Annulus rupture ($n=1$)
Edwards: 1
CoreValve: 0
Severe aortic regurgitation ($n=3$)
Edwards: 2
CoreValve: 1
Aortic dissection ($n=1$)
Edwards: 0
CoreValve: 1
Severe vascular bleeding ($n=1$)
Edwards: 1
CoreValve: 0

LV, left ventricle.

The need for a new definitive pacemaker implantation was significantly higher in the CoreValve treated patients compared to the Edwards treated patients. The incidence of renal failure (meaning dialysis needed), clinical stroke or transient ischemic attack (TIA) within the first month after TAVI was comparable between both treatment groups.

One-month survival was 88% for the Edwards and 89% for the CoreValve treated patients (NS). Causes of mortality are summarized in Table 5 and almost equally distributed between cardiac and non-cardiac reasons.

3.3. One-year clinical events and survival

One year clinical outcome data are summarized in Fig. 1. Overall one-year survival was 78% in the CoreValve transfemoral treated patients, 100% in the CoreValve subclavian treated patients, 82% in the Edwards transfemoral treated patients and 63% in the Edwards transapical treated patients. Causes of mortality within the first year are summarized in Table 5 and mainly related to non-cardiac reasons.

3.4. Edwards Sapien transfemoral vs. transapical treated patients: patient characteristics and long-term outcome

Data are summarized in Table 6 and Fig. 1. One-year survival of the transapically treated Edwards Sapien patients was significantly less compared to the transfemorally treated patients.

3.5. One-year echographic follow-up

Data are summarized in Fig. 2 and based on complete one-year echographic follow-up in 117 patients (60 CoreValve and 57 Edwards Sapien). Post-procedural transaortic pressure gradients were markedly low in both groups. During the first year after TAVI, no significant deterioration of the gradients was documented. No prosthetic structural deterioration or non-structural dysfunction was observed.

4. Discussion

Waiting final conclusions of randomized trials, carefully performed national registries, monitoring acute and long-term safety and efficacy results, both of CoreValve (transfemoral, subclavian) and Edwards (transfemoral, transapical) TAVI treated patients are of importance in

Table 4. One month outcome data

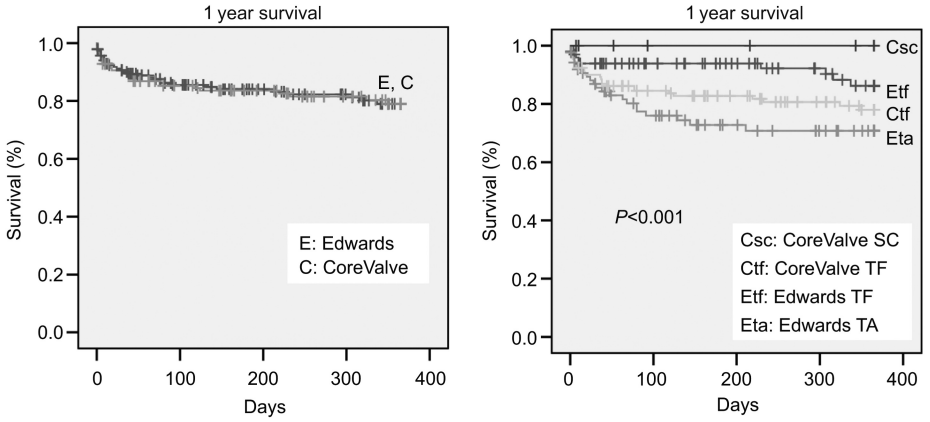
n (%)	Edwards Sapien	CoreValve	Total population	P-value
New pacemaker	9/181 (5)	31/138 (22)	40/319 (13)	0.000
Renal failure needing dialysis	10/181 (6)	9/138 (7)	19/319 (6)	0.096
Clinical stroke	9/181 (5)	5/138 (4)	14/319 (5)	0.67
TIA	2/181 (1)	1/138 (1)	3/319 (1)	0.57
One-month survival	165/187 (88)	126/141 (89)	291/328 (89)	0.99
One-month mortality	22/187 (12)	15/141 (11)	37/328 (11)	0.99

TIA, transient ischemic attack.

Table 5. Causes of mortality (procedural mortality not included)

$n=28$	Cardiac ($n=15$)	Non-cardiac ($n=13$)
<1 Month	Late tamponade (3)	Stroke or IC bleeding (5)
	Conduction disturbances with arrest (4)	Ischemic colitis (1)
	AR-heart failure (2)	Multi-organ failure (2)
	Heart failure (3)	Pneumonia – sepsis (3)
	Sudden death (3)	Bleeding complications (2)
$n=28$	Cardiac ($n=8$)	Non-cardiac ($n=20$)
1 Month–1 year	Heart failure (5)	Pneumonia (5)
		Acute resp failure (2)
	Sudden death (3)	(uro)Sepsis (3)
		Endocarditis (2)
		Late stroke (3)
		Astrocytoma (1)
		Trauma – IC bleeding (1)
		Hip fracture (3)

AR, aortic regurgitation; IC, intracranial.



%	CoreValve	Edwards TF	Edwards TA
1 month survival	91	94	86
6 month survival	82	91	71
1 year survival	79	82	63

Fig. 1. Kaplan–Meier survival curves, expressing one-year survival after TAVI. TAVI, transcatheter aortic valve implantation; TF, transfemoral; TA, transapical; SC, subcalvian.

understanding better possible clinical value of this new treatment modality for high-risk patients.

4.1. The Belgian TAVI Registry

The Belgian TAVI Registry is a carefully conducted prospective, non-randomized multicenter national registry, aiming to include and follow-up all Belgian TAVI procedures. In contrast to some other national or single centre registries, all consecutive TAVI patients in Belgium, both treated by the Edwards Sapien valve or by the CoreValve prosthesis, are included in this registry. Moreover, mid-term follow-up was completed in a very high number of patients. If possible, the reason of death was documented. Although there is no formal central core laboratory, both the Belgian Working Group for Interventional Cardiology and the Belgian Working Group for Cardiac Surgery stimulated participating sites for providing high-quality patient data.

Table 6. Edwards Sapien transfemoral vs. transapical

Patient characteristics	Edwards Sapien transfemoral ($n=99$)	Edwards Sapien transapical ($n=88$)	*P*-value
Age (years)	84±5	82±6	0.011
LVEF (%)	51±16	51±14	0.98
Log EuroSCORE (%)	29±15	33±17	0.101
Carotid dis *n* (%)	11 (11)	16 (14)	0.020
Diabetes *n* (%)	10 (10)	19 (18)	0.31
PVD *n* (%)	4 (4)	34 (30)	0.000
Porcelain ao *n* (%)	2 (2)	5 (4)	0.000
Prev CABG *n* (%)	5 (5)	20 (18)	0.002
One month MACE			
Pacemaker *n* (%)	4/96 (4)	5/85 (6)	0.19
Renal failure *n* (%)	2/96 (2)	8/85 (9)	0.005
Stroke *n* (%)	2/96 (2)	7/85 (8)	0.047

LVEF, left ventricular ejection fraction; PVD, peripheral arterial disease; ao, aorta; prev CABG, previous coronary artery bypass grafts; carotid dis, carotid disease.

4.2. Procedural results and one-month clinical events and survival

After careful selection of patients with severe symptomatic aortic valve stenosis, refused for surgery and with acceptable additional technical evaluation, TAVI can be successfully performed in a high number of patients, with low procedural mortality. This finding is confirmed by many other similar registries [1–4]. The main reasons for procedural mortality are related to suboptimal guidewire manipulation [leading to left ventricle (LV) perforation], suboptimal aortic root measurements (leading to severe aortic valve regurgitation or annulus rupture) or major vascular complications (bleeding or dissection).

One-month mortality after TAVI is almost equally distributed between cardiac and non-cardiac causes. Three patients died due to suboptimal manipulation of the temporary pacing electrode with severe tamponade and collapse, while at least four others died due to too rapid removal or dislocation of the pacing electrode with occurrence of conduction disturbances and arrest. This finding focuses our attention to the need of improved post-procedural care and better and more uniform guidelines to pacemaker management after TAVI. Another two to five patients died within the first weeks after TAVI due to severe aortic valve regurgitation related to valve/annulus mismatch or valve undersizing. This finding focuses on even

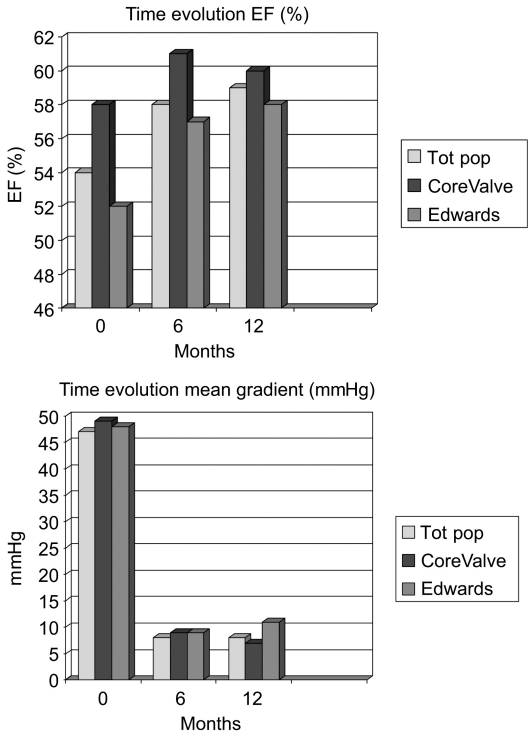


Fig. 2. Echocardiographic follow-up of LV function (ejection fraction, EF) and mean aortic valve gradient during the first year after TAVI. TAVI, transcatheter aortic valve implantation; LV, left ventricle.

more careful technical selection (evaluation of aortic root dimensions) of potential TAVI patients. Finally, 13 patients died due to non-cardiac complications of which some (pneumonia, sepsis, ...) are probably related to too high frailty of selected patients.

4.3. Mid-term outcome after TAVI

One-year survival in this high-risk population is good, mainly in the transfemorally and subclavian (only limited group) CoreValve treated patients and the transfemorally treated Edwards Sapien patients. Survival rates are probably significantly more, than what was predicted by different risk scores in this patient population. Our registry demonstrates that causes of mid-term mortality are mainly (20/28) related to age-dependent complications and are probably not related to, or cannot be prevented by TAVI. Long-term cardiac mortality seems to be relatively low after TAVI, in a patient population which was initially strongly symptomatic with high chance of cardiac death.

Although non-randomized registries are not designed to compare different treatment strategies, a remarkable observation in our registry is the significantly higher mid-term mortality of the transapically treated Edwards Sapien patients, compared to the transfemorally treated Edwards Sapien patients and the CoreValve treated patients. Whether this is related to different baseline patient characteristics or to other procedural elements, cannot be answered by our data.

4.4. Limitations

There were no centres performing both CoreValve and Edwards procedures. The number of patients is relatively limited, comparison of treatment strategies (Edwards Sapien vs. CoreValve) (transfemoral vs. transapical) is not mandatory in a non-randomized registry and there is no central core laboratory monitoring all events.

5. Conclusions

Percutaneous aortic valve replacement for selected patients with severe aortic valve stenosis is associated with a low acute and mid-term mortality in a high-risk population. Further progress in better technical patient selection, careful post-procedural care and evaluation of most optimal access are essential to improve actual results.

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Conference discussion

Dr. M. Antunes (*Coimbra, Portugal*): *Dr. Bosmans* and colleagues, here represented by Dr. Rodrigus, analyzed the Belgian prospective non-randomized multicenter registry of transcatheter aortic valve implantation (TAVI), an emerging alternative for high-risk symptomatic patients with severe aortic stenosis. The report included 328 consecutive high-risk symptomatic patients, mean age 83 years and a logistic EuroSCORE of 28. There was a high-procedural success of 97%, and one-month survival of 91% for both types of valves. Overall, one-year survival was a little bit lower for the transapically-treated patients.

These results are in keeping with current reports coming from most other centers and prove the feasibility and reproducibility of the procedure, at least in selected centers, but still leave open the question of median to long-term results in comparison with the classical surgical AVR. Of importance, the paper does not give an insight into the number and percentage of both techniques, and, even more importantly, does not shed any light on the numbers and results of patients originally referred for TAVI because of a too high-risk for surgery and ultimately operated on. Many recent series of TAVI include groups of these patients who had better results than those of the TAVI groups. I believe it is time to make a wide survey of both groups, which would constitute the closest approximation to randomization that we have until now.

As with other studies, this one bases its referral for TAVI on the logistic EuroSCORE, which has now been clearly demonstrated to be of no value in accurately predicting the risk of AVR because it consistently over-predicts it by a factor of three or four, especially in the high-risk groups. And it is interesting that the authors did not use the additive EuroSCORE or the STS score (Society of Thoracic Surgeons), which are viewed as more accurate. This could be interpreted as deliberate and, in my opinion, unfair, in my opinion, not to say unethical, in bedevilling the surgical procedure for these patients.

I have a couple of questions, then. The authors observed the usual high incidence of 23% requirement for pacemaker implantation, 6% incidence of stroke and TIA, and 6% incidence of renal failure. What are the reasons for persisting with this valve, especially in view of the high incidence of pacemaker requirement? Did you detect any advantage of one valve versus the other since you have a large number for comparison of both valves?

Surprisingly for a selected group of patients and therefore closely followed, the authors report an unknown cause of death in 14 early and, in the paper, 12 first-year deaths, nearly half of the total number of deaths. For a registry, this is too high an incidence of death from unknown cause. What are the reasons for this?

Finally, in the paper you state that the late mortality is essentially due to age-related non-cardiac complications, but in this you included causes such as endocarditis and stroke. Are these not cardiac-related? In many surgical series reported, these would certainly be classified as such.

Dr. Rodrigus: The choice of the valve is a center decision. It has to do with the concept of the valve and the belief you have in one of the two concepts, I think. Furthermore, there are other issues playing a role, not only the financial question. So that is a center decision. And I do not think the high pacemaker need is reason not to use the CoreValve device.

And concerning the registration of mortality, this is a Belgian problem. We do not have the same kind of databases as the UK. This registry started in the first place to look at one-month median survival, and then obviously it was of interest to have a longer follow-up. So we can only thank the participants for trying to send in their data, but not every center is very keen on finding out the cause of mortality of its patients.

Dr. M. Sousa Uva (*Lisbon, Portugal*): First question, have the Belgian authorities changed their minds with these results? Because, as people maybe do not know, the Health Technology Assessment in Belgium has considered that TAVI should not be reimbursed. So that is my first question.

The second question. With these results, have the Belgian health authorities changed their policy and now reimburse this procedure?

Dr. Rodrigus: No, not yet. Last year they stated that they will await the results of the PARTNER trial. So we are hoping these results are very good and that they will reimburse it.