Transcatheter aortic valve implantation in patients with severe aortic valve stenosis and large aortic annulus, using the self-expanding 31-mm Medtronic CoreValve prosthesis: First clinical experience

Freek Nijhoff, MD,^a Pierfrancesco Agostoni, MD, PhD,^a Hafid Amrane, MD,^b Azeem Latib, MD,^c Luca Testa, MD, PhD,^d Jacopo A. Oreglia, MD,^e Federico De Marco, MD,^e Mariam Samim, MD,^a Francesco Bedogni, MD,^d Francesco Maisano, MD,^c Giuseppe Bruschi, MD, FESC,^e Antonio Colombo, MD,^c Ad J. Van Boven, MD, PhD,^b and Pieter R. Stella, MD, PhD^a

Objectives: With the introduction of the 31-mm Medtronic CoreValve prosthesis, patients with large aortic annulus have become eligible for transcatheter aortic valve implantation. The aim of this study was to evaluate the feasibility, efficacy, and safety of transcatheter aortic valve implantation using the 31-mm Medtronic CoreValve in patients with severe aortic valve stenosis and large aortic annulus.

Methods: Five institutions in the Netherlands and Italy participated in a retrospective multicenter registry. Clinical, procedural, and imaging data of patients treated with the 31-mm Medtronic CoreValve were retrospectively collected in accordance with the Valve Academic Research Consortium-2 criteria.

Results: Between August 2011 and November 2012, 47 patients (44 men, mean age 77.6 ± 8.9 years) received the 31-mm Medtronic CoreValve prosthesis for severe aortic stenosis. Device success (correct positioning of a single valve with intended performance and no all-cause 30-day mortality) was achieved in 31 patients (66.0%). Reasons for failing the device success criteria were significant prosthetic aortic regurgitation in 3 patients (6.4%), second valve implantation in 10 patients (21.2%) (8 cases of malpositioning with high-grade aortic regurgitation, 1 acute valve dislocation, and 1 delayed valve dislocation), 1 of whom died intrahospital, and in-hospital mortality in a further 3 patients (6.4%). Peak and mean transaortic gradients decreased significantly ($P < .01$). The rate of new pacemaker implantations was 41.7%.

Conclusions: In this retrospective multicenter registry, transcatheter treatment of severe aortic valve stenosis with the 31-mm Medtronic CoreValve seemed to be challenging, even in experienced hands. If the prosthesis is properly implanted, it offers adequate valve hemodynamics and proper functioning. (J Thorac Cardiovasc Surg 2014;148:492-9)

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Transcatheter aortic valve implantation (TAVI) is a rapidly evolving treatment modality for patients with symptomatic

severe aortic valve stenosis (AS), significantly improving survival and quality of life.^{1,2} Current application of TAVI is confined to patients with prohibitive or high risk for surgical aortic valve replacement (SAVR),³ although trials involving intermediate-risk patients are ongoing.⁴ Until recently, another constraint to the practice of TAVI was the limited range of prosthesis sizes. Patients with severe AS and large aortic annulus (diameter > 27 mm), otherwise suitable for TAVI, had to be denied transcatheter treatment because no adequately sized prostheses were available.⁵ In response to the clinical need for a larger valve prosthesis, the self-expanding 31-mm Medtronic CoreValve (MCV31; Medtronic Inc., Minneapolis, Minn) has been developed. With the introduction of this device, patients with an aortic annulus dimension up to 29 mm in diameter have become eligible for TAVI. However, the clinical use of this larger prosthesis may enhance the procedural challenges. As only the basal inflow portion of the stent frame has a 31-mm profile, there is little margin for proper valve placement, rendering valve positioning more decisive to achieve a good implantation result. Furthermore, the bulky stent frame may increase the risk of interference with mitral valve

From the Department of Cardiology,^a University Medical Center Utrecht, Utrecht, The Netherlands; Medisch Centrum Leeuwarden,^b Afdeling Hartcatheterisatie, Leeuwarden, The Netherlands; San Raffaele Scientific Institute,^c Milan, Italy; Istituto Clinico Sant' Ambrogio,^d Milan, Italy; and Ospedale Niguarda Ca' Granda,^e Milan, Italy.

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Drs Nijhoff and Agostoni equally contributed to this article.

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Address for reprints: Pieter R. Stella, MD, PhD, Department of Cardiology, University Medical Center Utrecht, Heidelberglaan 100, Room E.04.210, 3584 CX, Utrecht, The Netherlands (E-mail: p.stella@umcutrecht.nl).

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Abbreviations and Acronyms

AR	= Aortic regurgitation
AS	= Aortic valve stenosis
CE	= Conformité Européenne
MSCT	= Multislice computer tomography
NYHA	= New York Heart Association
SAVR	= Surgical aortic valve replacement
TAVI	= Transcatheter aortic valve implantation
TEE	= transesophageal echocardiography
TTE	= transthoracic echocardiography
VARC-2	= Valve Academic Research Consortium-2

function⁶ and damage to the cardiac conduction system during prosthesis deployment.⁷ So far, no studies regarding clinical experiences with the MCV31 have been published. The aim of this study was to investigate the safety, efficacy, and in-hospital outcomes of TAVI using the MCV31 device.

METHODS

For a comprehensive description of the study methodology, please refer to the online [supplementary methods section](#).

Study Design

This study is an observational, retrospective, multicenter, single-arm registry. All patients who underwent TAVI for severe aortic valve disease using the MCV31 device were retrospectively identified. Patients selected for TAVI had been considered unsuitable for SAVR by consensus of a cardiologist and a cardiac surgeon, because of a high predicted operative mortality risk (logistic EuroSCORE >15) or the presence of absolute contraindications for SAVR (eg, porcelain aorta). Further details on patient selection have been published previously.³ Patient data were retrospectively collected and documented in a registry. All patients gave informed consent for the procedure and because of the retrospective nature of the study design, ethics committee approval was waived.

Device and Implantation Procedure

The MCV31 device received CE (Conformité Européenne) approval in August 2011 for transfemoral, transaxillary, and direct aortic implantation, and has roughly the same design characteristics as its smaller 26-mm and 29-mm predecessors.⁸ It is only the stent frame inflow portion of the MCV31 that is larger compared with the 29-mm prosthesis, giving rise to a pronounced tapering of the inflow portion ([Figure 1](#)). Therefore, correct placement, high enough to allow proper apposition of the enlarged inflow part to the native aortic valve, is more critical than with the smaller sizes. The TAVI procedures were performed via the transfemoral, transaxillary, or direct aortic approach according to the choice of the operators, with standard access techniques,^{9,10} under general anesthesia or conscious sedation. The implantation result (valvular function and location) was assessed by angiography and echocardiography (either transthoracic echocardiography [TTE], transesophageal echocardiography [TEE] or intracardiac echocardiography).

End Point Definitions

In-hospital complications were registered in concordance with the recently published Valve Academic Research Consortium-2 (VARC-2) consensus document.¹¹ Device success was defined accordingly as the

proper implantation of the first valve prosthesis used, with intended performance of the prosthetic heart valve (peak aortic flow velocity <3 m/s and no moderate or severe aortic regurgitation [AR]) and no procedural mortality (30-day all-cause mortality).

Statistical Analysis

All data were analyzed using IBM SPSS Statistics software version 20 (IBM Corp., Armonk, NY). Results for continuous variables are presented as means $\pm$ standard deviation or medians [interquartile range], as considered appropriate. Categorical variables are reported as counts and percentages. The comparison of continuous variables was done using the Student *t* test for unpaired measures or paired *t* test for repeated measures or their nonparametric equivalents, the Mann-Whitney *U* test, and the Wilcoxon signed ranks test, where appropriate. Categorical variables were analyzed using the χ^2 or Fisher exact test.

RESULTS

Between the CE approval of the MCV31 in August 2011 and November 2012, 440 patients underwent TAVI at 5 participating institutions in the Netherlands and Italy. All centers were well experienced in CoreValve implantations (23, 26, and 29 mm) when the MCV31 was introduced. Fifty-four patients (12.3%) received the MCV31 device. Seven patients were excluded from the study because of off-label use of the prosthesis for pure severe AR without AS, leaving 47 patients for further analysis. Most of the patients were male (93.6%); the mean age was 77.6 ± 8.9 years, ranging from 48 to 90 years. Further baseline characteristics are listed in [Table 1](#). The mean aortic annulus diameter (average annulus diameter, as derived from the maximum and minimum diameters) was 26.4 ± 2.7 mm on TEE and 27.3 ± 1.6 mm on multislice computer tomography (MSCT). Overall left ventricular function was depressed; 24 patients (44.5%) exhibited a left ventricular ejection fraction less than 40%. Preprocedural imaging findings are summarized in [Table 2](#).

Procedural Results

Most patients underwent TAVI through a transfemoral approach (36 patients), 6 patients were treated via direct aortic access, and 5 patients underwent a transaxillary procedure. Acute procedural success (such as that shown in [Figure 2, A](#)) was achieved in 36 patients (76.6%). One intra-procedural death occurred, caused by ascending aortic dissection resulting in cardiac tamponade during a transfemoral procedure. In 1 patient, the valve prosthesis acutely embolized to the ascending aorta, which was adequately managed by snare catheter fixation and relocation of the prosthesis in the ascending aorta, followed by implantation of a second valve prosthesis in series ([Figure 2, C and D](#)).

Twenty-two patients (46.8%) demonstrated significant paravalvular AR (grade 2 or higher) immediately after valve deployment. In 9 of these patients (19.1%), significant paravalvular AR occurred as a consequence of incorrect valve placement, exclusively concerning too low implantations ([Figure 2, B](#)). Seven of these patients required implantation

FIGURE 1. Medtronic CoreValve range of prostheses. The CoreValve third-generation range of prostheses with corresponding stent frame dimensions and manufacturer recommendations for MSCT-based sizing. MSCT, Multislice computer tomography.

of a second valve prosthesis (TAV-in-TAV) in the same setting, 1 patient received TAV-in-TAV implantation during a second procedure, and 1 patient was treated with snare catheter repositioning only (correct annular placement was achieved by gently pulling the prosthesis upwards,

TABLE 1. Baseline characteristics

	Number (%) (N = 47)*
Age, y	77.6 ± 8.9
Female	3 (6.4)
Body mass index, kg/m ²	26.7 ± 4.7
Length, cm	173.0 ± 7.5
Weight, kg	80.1 ± 14.0
Body surface area, m ² †	1.95 ± 0.19
Diabetes mellitus	12 (25.5)
Hypertension	30 (63.8)
Dyslipidemia	23 (48.9)
COPD	20 (42.6)
Chronic renal disease	20 (42.6)
Glomerular filtration rate, mL/min‡	58.6 ± 21.4
Cerebrovascular disease	13 (27.7)
Peripheral artery disease	18 (38.3)
Coronary artery disease	30 (63.8)
Previous myocardial infarction	11 (23.4)
Previous PCI	21 (44.7)
Previous CABG	9 (19.1)
Atrial fibrillation	16 (34.0)
Previous pacemaker implantation	11 (23.4)
Heart rhythm	
Sinus rhythm	35 (74.5)
Atrial fibrillation	7 (14.9)
Pacemaker rhythm	5 (10.6)
NYHA functional class ≥III	37 (78.7)
Logistic EuroSCORE§ (%)	24.7 ± 23.3
Prohibitive high risk for surgery	32 (68.1)

COPD, Chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; NYHA, New York Heart Association; EuroSCORE, European System for Cardiac Operative Risk Evaluation. *Results are given as the number (%) except where indicated otherwise. †Calculated using the Mosteller formula. ‡Estimated with the Modification of Diet in Renal Disease formula. §Operative risk as assessed by the EuroSCORE I. ||Defined as a logistic EuroSCORE ≥15.0%.

TABLE 2. Preprocedural imaging

	N = 47
Left ventricular ejection fraction (%)	43.8 ± 14.7
Left ventricular ejection fraction <40%, n (%)	19 (40.4)
Peak aortic transvalvular pressure gradient (mm Hg)	68.5 ± 23.8
Mean aortic transvalvular pressure gradient (mm Hg)	40.1 ± 15.9
Aortic valve orifice area (cm ²)	0.69 ± 0.19
Aortic valve regurgitation grade 2 or higher, n (%)	13 (27.7)
Mitral valve regurgitation grade 2 or higher	11 (23.4)
Systolic pulmonary artery pressure (mm Hg)	40.4 ± 10.9
Pulmonary artery hypertension (sPAP ≥ 60 mm Hg), n (%)	4 (8.5)
Aortic annulus diameter on TEE (mm)	26.4 ± 2.7
Aortic annulus average diameter on MSCT (mm)*	27.3 ± 1.6 (range 25.5-30.5)
Percentage of oversizing†	12.2 ± 4.7

sPAP, Systolic pulmonary arterial pressure; TEE, transesophageal echocardiography; MSCT, multislice computer tomography. *Average diameter calculated using the formula (maximum diameter + minimum diameter)/2. †As calculated by the formula (prosthesis diameter – average diameter on MSCT)/prosthesis diameter.

although moderate paravalvular AR persisted). In another 12 patients (25.5%), significant paravalvular AR was successfully addressed by postdilatation, because prosthesis underexpansion was the underlying cause. In the remaining patient, grade 2 AR did not improve after postdilatation and was accepted, considering the risk of additional postdilatation. An overview of the procedural variables is given in Table 3.

Echocardiographic Results

All patients underwent TTE before discharge (Table 4), except for the patient who died during the procedure. Peak and mean aortic transvalvular pressure gradients decreased from 68.5 ± 23.8 mm Hg and 40.1 ± 15.9 mm Hg at baseline to 18.0 ± 6.3 mm Hg and 9.9 ± 3.7 mm Hg after TAVI, respectively (both $P < .001$). PredischARGE echocardiography showed AR in 32 patients (71.7%): mild in 25 patients (54.3%), moderate in 6 patients (13.0%), and severe in 1 patient (2.2%). The origin of post-procedural AR was predominantly paravalvular (29 of 32 cases) and less often transvalvular or mixed. The degree of mitral valve regurgitation (MR) decreased in 8 patients (17.4%), remained unchanged in 27 patients (57.4%), worsened in 7 patients (15.2%), and was inadequately assessed in the remaining patients. Worsening of the degree of MR was not related to too low implantations that required TAV-in-TAV implantation. The change in the distribution of MR severity before and after TAVI was not significant ($P = .64$), the proportion of patients with important MR (grade 2 or higher) remained the same.

In-Hospital Outcome

There were 4 in-hospital deaths (8.5%), including the case of aortic dissection described earlier. One patient, with

FIGURE 2. MCV31 implantation. A, Angiographic result after correct implantation of a 31-mm CoreValve, demonstrating mild paravalvular AR; B, CoreValve implanted too low with severe periprosthetic AR; C, introduction of a second prosthesis after spontaneous acute embolization of an MCV31 toward the ascending aorta; D, the result after CoreValve implantation in series.

preexisting poor left ventricular function, died of congestive heart failure induced by pneumonia, despite good valve prosthesis function. Another patient died of sequelae of delayed valve dislocation. On the sixth postprocedural day, the patient developed acute cardiac failure with respiratory insufficiency requiring intubation. Echocardiography revealed new severe AR, raising the suspicion of valve dislocation. On emergency angiography, downward displacement of the CoreValve toward the left ventricular outflow tract was diagnosed (Figure 3, A-C), which was subsequently treated with TAV-in-TAV implantation of a smaller 29-mm CoreValve. Despite the successful procedure, the patient died of progressive coma probably caused by hypoxic cerebral damage. In 1 patient, the cause of death could not be established because death occurred after unsuccessful resuscitation (pulseless electrical activity) and no autopsy was performed. No additional 30-day mortality was reported.

In-hospital re-TAVI was performed in 2 patients. One patient underwent successful re-TAVI to address significant AR resulting from a too low implantation during the first procedure (as mentioned earlier). The other re-TAVI was performed in the case of delayed valve dislocation described earlier.

There were 2 cases of in-hospital stroke (4.2%), both ischemic events. Of the 36 patients without previous pacemaker implantation, 15 (41.7%) received a new pacemaker implantation after TAVI, mainly because of third-degree atrioventricular block ($n = 13$). Other pacemaker indications were sick-sinus syndrome ($n = 1$) and bradycardia in atrial fibrillation ($n = 1$). Further data on in-hospital outcomes and echocardiographic results are outlined in Table 4.

Device Success

Device success was achieved in 31 patients (66.0%). Reasons for not fulfilling the device success criteria were moderate or severe prosthetic AR in 3 patients (6.4%); second valve implantation in 10 patients (21.2%), 1 of whom died in hospital; and in-hospital mortality in an additional 3 patients (6.4%).

Univariate Analysis

A composite end point for malpositioning (suboptimal placement of the valve) was created for use in univariate analysis, including too low implantations requiring second valve implantation or snare catheter repositioning, and

TABLE 3. Procedural data

	Number (%) (N = 47)*
Approach	
Transfemoral	36 (76.6)
Direct aortic	6 (12.8)
Transaxillary	5 (10.6)
General anesthesia	11 (23.4)
Fluoroscopy time, minutes (median [interquartile range])	22.5 [11]
Predilatation	31 (66.0)
Predilatation balloon size, mm	24.6 ± 1.8
Use of stabilizing ventricular pacing	22 (46.8)
Requirement of postdilatation	15 (31.9)
Snare catheter repositioning	1 (2.1)
Conversion to surgery	0
Use of extracorporeal circulation	0
Acute procedural success†	36 (76.6)
Second valve implanted	8 (17.0)
Aortic regurgitation grade 2 or higher	2 (4.3)
Intraprocedural death	1 (2.1)

*Results are given as the number (%) except where indicated otherwise. †Successful implantation of a single valve with proper functioning (correct anatomic position of the valve with no moderate or severe AR present) and the patient leaving the operating room alive.

acute and delayed valve dislocations. None of the variables analyzed showed a statistically significant association with the end point (Table 5). However, predilatation was nonsignificantly more often performed in patients free of

TABLE 4. Outcome and predischARGE echocardiographic data

	Number (%) (N = 47)*
In-hospital outcome	
Mortality	4 (8.5)
Stroke	2 (4.3)
Myocardial infarction	0
Bleeding	4 (8.6)
Vascular complications	2 (4.3)
New permanent pacemaker implantation	15 (41.7)
Acute kidney injury (stage I)†	7 (14.9)
Delayed valve dislocation	1 (2.1)
Re-TAVI	2 (4.3)
Length of hospital stay, days (median [interquartile range])	6 [3]
Device success	31 (66.0)
Postprocedural echocardiography (N = 46)	
Left ventricular ejection fraction <40%	19 (41.3)
Peak aortic transvalvular pressure gradient, mm Hg	17.4 ± 6.0
Mean aortic transvalvular pressure gradient, mm Hg	9.6 ± 3.8
Aortic regurgitation grade 2 or higher	7 (14.9)
Mitral valve regurgitation grade 2 or higher	10 (21.7)
30-d mortality‡	4 (8.5)

TAVI, Transcatheter aortic valve implantation. *Results are given as the number (%) except where indicated otherwise. †Stage I acute kidney injury: 1.5-1.99 times increase in serum creatinine level compared with baseline, or an absolute increase of >26.4 µmol/L (Acute Kidney Injury Network classification). ‡Cumulative 30-day mortality.

malpositioning, with a trend toward more aggressive predilatation (with bigger balloons) in this patient group.

DISCUSSION

This multicenter registry is the first to publish on clinical experiences with the MCV31 prosthesis for transcatheter treatment of severe aortic valve disease in patients with a large aortic valve annulus (>27 mm). In this registry, these patients could be further characterized by male gender and depressed left ventricular function, which is in line with recent insights on left ventricular dysfunction being an independent predictor of a large annulus.¹² This situation stresses the importance of the availability of a large-valve prosthesis, as sufficient oversizing must be provided to decrease the amount of paravalvular AR in this vulnerable patient category.¹³ The MCV31 certainly fills a clinical need; this registry shows that this larger valve is indicated in up to 12% of patients suitable for TAVI. In the following paragraphs, the feasibility, efficacy, and safety of the MCV31 are discussed.

Feasibility

Over the years, transcatheter implantation of the Medtronic CoreValve has been performed with increasing success, reflecting evolving delivery techniques and operator experience.⁸ Several large registries have reported excellent procedural success rates for third-generation 26-mm and 29-mm CoreValve implantations, reaching nearly 98%.^{14,15} The results for MCV31 implantations reported in this study are at odds with this trend, as the need for second valve implantations had a major impact on the acute procedural success rate. The incidence of second CoreValve implantation was high (17.0%) compared with those reported in the real-world FRANCE2 and Sentinel registries (3.5% and 2.6%, respectively).^{14,16} Second valve implantation was predominantly due to cases of too low first valve implantation, known to be the most common type of suboptimal CoreValve deployment causing significant paravalvular AR.¹⁷ Too low implantation of the prosthesis may lead to severe periprosthetic leakage, by leaving a gap between the aortic annulus plane and the pericardial skirt covering the prosthesis stent frame. TAV-in-TAV implantation is an established technique to address the problem of a low implant; snare catheter repositioning may be considered in some cases.¹⁷ Device success, as defined by VARC-2, decreased further in this registry as 1 case of delayed valve dislocation was observed, requiring re-TAVI. No previous reports on delayed dislocation after CoreValve implantation could be found. CoreValve dislocation is exclusively reported in the acute setting, occurring as valve embolization toward the ascending aorta, immediately after implantation or during snaring maneuvers.^{18,19}

FIGURE 3. Delayed valve dislocation. A, Initial MCV31 implanted a little low. B, Angiography in the same patient 6 days later; the MCV31 was dislocated toward the left ventricle. C, Angiographic result after a TAV-in-TAV procedure.

TABLE 5. Univariate analysis

Variable	No malpositioning, n (%) (N = 35)*	Malpositioning, n (%) (N = 11)	P value
Predictors for malpositioning			
Preprocedural LVEF, %	45.8 ± 14.3	37.9 ± 15.8	.11
Preprocedural grade AR, median [interquartile range]	1.0 [1.0]	1.0 [2.0]	.57
Average annulus diameter, mm	27.2 ± 1.6	27.5 ± 1.6	.66
Aortic annulus >29 mm	1 (2.8)	1 (9.1)	.42
Percentage of oversizing†	12.5 ± 4.7	11.2 ± 5.0	.34
Annulus eccentricity‡	0.17 ± 0.09	0.13 ± 0.09	.15
Transfemoral approach	26 (74.3)	9 (81.8)	1.00
Predilatation	25 (71.4)	5 (45.5)	.15
Balloon size, mm (median [interquartile range])	25.0 [2]	23.0 [3]	.14
Balloon to annulus ratio§	0.92 ± 0.08	0.89 ± 0.05	.45
Stabilizing ventricular pacing	16 (47.1)	5 (45.5)	.92
Effect on outcome			
Fluoroscopy time, minutes (median [interquartile range])	21 [12]	27 [15]	.07
Mortality	2 (5.7)	1 (9.1)	1.00
Stroke	1 (2.8)	1 (9.1)	.42
New permanent pacemaker implantation	11 (39.3)	2 (20.0)	.44
Acute kidney injury	4 (11.1)	3 (27.3)	.33
Length of hospital stay, days (median [interquartile range])	6 [3]	7 [9]	.13

LVEF, Left ventricular ejection fraction; AR, aortic regurgitation. *Excluding the patient who had aortic dissection and died before valve implantation. †Calculated using the formula $([\text{prosthesis diameter} - \text{average diameter}]/\text{prosthesis diameter}) \times 100$. ‡Calculated using the formula $1 - (\text{minimal diameter}/\text{maximal diameter})$, where 0 indicates the annulus is a perfect circle. §Ratio of the balloon diameter and aortic annulus average diameter; increases as the balloon gets more oversized. ||Excluding patients with previous pacemaker implantation.

All cases of malpositioning encountered in this registry involved a too low position of the MCV31, occurring either acutely (initial too low implantation) or in a later phase (delayed dislocation toward the left ventricle). This finding may indicate an operator tendency for too low valve positioning, although local experience with other CoreValve sizes is not supportive. Otherwise, it may reflect an intrinsic property of the MCV31 to creep into the left ventricle during deployment and maybe even during the following days, as stent frame expansion continues. Prosthesis design may contribute to this phenomenon, as the pronounced tapering

of the stent frame inflow portion (producing an increasingly acute angle α , absent in the smaller CoreValves) may act like an expandable dowel during expansion, pulling the prosthesis deeper into the left ventricular outflow tract (Figure 1). Because only the most distal part of the inflow portion has a diameter of 31 mm, the valve should be implanted higher in the annulus than the smaller diameter valves.

The decision to incorporate too low implantation as well as valve dislocation in a composite malpositioning end point was based on the assumption that both complications may share suboptimal valve positioning as an underlying mechanism (although valve implantation height was not quantified). None of the variables used in the univariate analysis was significantly related to this end point. However, predilatation was more frequently applied in patients free of the composite malpositioning end point, with a modest trend toward more aggressive predilatation with larger balloons and a larger balloon to annulus ratio. Depressed left ventricular function may have been an important argument for omitting predilatation in patients in the malpositioning group, because impaired left ventricular function may be more sensitive to rapid pacing during predilatation. Predilatation has been considered a mandatory step in TAVI for some time, because it fractures valve calcifications and increases the effective orifice area, thereby facilitating an even deployment of the valve prosthesis. This concept is not supported by the literature, however; a feasibility study prospectively omitting predilatation in CoreValve procedures reported excellent results with achievement of technical success in 96.7% of 60 patients.²⁰ Multivariate analysis on predictors of malpositioning was not performed as the sample size was too small to generate robust data.

Efficacy

Postimplantation valve hemodynamics were good, considering the substantial significant decrease in both mean and peak transaortic gradients. None of the patients had residual stenosis on predischARGE TTE. The incidence and distribution of paravalvular AR were satisfactory, although postdilatation, snaring and/or second valve implantation were indicated in half of the cases. The second valve implantations in this study were highly efficacious for resolving severe paravalvular AR in case of too low implantations, reducing the severity of AR to mild in 7 of 8 patients. The durability and long-term safety of TAV-in-TAV procedures is yet to be established, but previously published 1-year outcomes are promising.¹⁷

Overall, moderate AR was present in 14.9% of patients on discharge, an incidence well within the range reported in a meta-analysis of SAPIEN and CoreValve devices.²¹ The incidence of moderate AR found in this study can be considered increased, however, as compared with the

recently published results of the Sentinel registry, reporting postprocedural moderate AR in 9.9% of patients treated with the CoreValve throughout 2011 and 2012.¹⁶

Safety

The rate of in-hospital death was 8.5% in this registry, which can be regarded as high, as was the 4.2% incidence of stroke. Delayed valve dislocation seemed to be a harmful complication, as 1 death was clearly related to the sequelae of this event. The sole case of intraprocedural mortality in this registry was caused by aortic dissection, a rare and dreadful complication often leading to death. Aortic dissection occurred after failed attempts to cross the native valve with the delivery catheter before prosthesis deployment, and therefore cannot be attributed to the MCV31 device.

The absence of myocardial infarction in this study was not surprising, as reduced MCV31 height may decrease the already uncommon occurrence of this complication. The rate of new permanent pacemaker implantation was at the high end of the range usually observed after CoreValve implantation.^{16,22} This may indicate a trend for lower device implantation in this cohort, as low placement is associated with conduction disorders after CoreValve procedures.²³ Alternatively, it may be conceivable that the tapered design of the valve inflow portion leads to a more localized exertion of radial pressure to the subvalvular structures during deployment, thereby increasing the likelihood of damaging the conduction system. In contrast to previous data, the incidence of pacemaker implantation was not related to too low first valve placement requiring TAV-in-TAV implantation.¹⁷

No clear unfavorable effect of the MCV31 on mitral valve function could be discerned, although a benefit on MR as seen after implantation of the Edwards SAPIEN valve was absent.²⁴ Despite increased potential for complications, acutely performed TAV-in-TAV procedures seemed to be safe in this cohort, because no additional morbidity or mortality was observed. Only a nonsignificant higher rate of stage 1 acute kidney injury was noted, probably caused by the exposure to higher volumes of contrast fluids.

Limitations

The present study is an observational, retrospective, multicenter, single-arm registry and therefore subject to all the shortcomings involved in retrospective research. MSCT and echocardiography images were not evaluated by a core laboratory, which may have led to heterogeneity in valve sizing and assessment of paravalvular AR. Because of the sample size and observational retrospective nature of the study, no firm conclusions can be drawn on the underlying cause of the low procedural success rates in this registry. The absence of a control group consisting of patients treated with smaller CoreValve sizes leaves uncertainty about whether the results are operator, patient, or prosthesis

dependent. No standard technique has been adopted for MCV31 implantation in this cohort; for example, no mandatory predilatation with prespecified balloon size or use of pacing during implantation was required. Furthermore, this registry is focused on procedural and in-hospital outcomes and offers no insights into mid-term and long-term safety and efficacy. Larger series of MCV31 implantations with longer duration of follow-up, preferably matched to a cohort of smaller CoreValves, are necessary for thorough evaluation of this prosthesis.

CONCLUSIONS

In this retrospective multicenter registry, transcatheter treatment of severe AS with the MCV31 device seemed to be challenging, even in experienced hands. The valve should be implanted higher in the annulus than the smaller (26 and 29 mm) CoreValves, because only the short inflow portion of the valve has a diameter of 31 mm. Device success was low, predominantly because of malpositioning requiring second valve implantation. The rate of new pacemaker implantations after the procedure was high. If the MCV31 is properly implanted, it offers adequate valve hemodynamics and proper functioning.

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References

- Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med*. 2010;363:1597-607.
- Reynolds MR, Magnuson EA, Lei Y, Leon MB, Smith CR, Svensson LG, et al. Health-related quality of life after transcatheter aortic valve replacement in inoperable patients with severe aortic stenosis. *Circulation*. 2011;124:1964-72.
- Holmes DR Jr, Mack MJ, Kaul S, Agnihotri A, Alexander KP, Bailey SR, et al. 2012 ACCF/AATS/SCAI/STS expert consensus document on transcatheter aortic valve replacement. *J Am Coll Cardiol*. 2012;59:1200-54.
- Genereux P, Head SJ, Wood DA, Kodali SK, Williams MR, Paradis JM, et al. Transcatheter aortic valve implantation 10-year anniversary: review of current evidence and clinical implications. *Eur Heart J*. 2012;33:2388-400.
- John D, Hausen S, Latsios G, Yucel S, Eberle HC, Farazandeh M, et al. Numerous patients fail the aortic annulus criteria in transcatheter aortic valve implantation - comparison of current devices. Poster presented at the 23rd Annual Symposium of the Transcatheter Cardiovascular Therapeutics, November 7, 2011; San Francisco, Calif.
- Cilingiroglu M, Hakeem A. Fate of mitral regurgitation following transcatheter aortic valve implantation. *Catheter Cardiovasc Interv*. 2011;78:645-6.
- Bleiziffer S, Ruge H, Horer J, Hutter A, Geisbusch S, Brockmann G, et al. Predictors for new-onset complete heart block after transcatheter aortic valve implantation. *JACC Cardiovasc Interv*. 2010;3:524-30.
- Grube E, Buellesfeld L, Mueller R, Sauren B, Zickmann B, Nair D, et al. Progress and current status of percutaneous aortic valve replacement: results of three device generations of the CoreValve Revalving system. *Circ Cardiovasc Interv*. 2008;1:167-75.
- Bruschi G, De Marco F, Fratto P, Oreglia J, Colombo P, Paino R, et al. Direct aortic access through right minithoracotomy for implantation of self-expanding aortic bioprosthetic valves. *J Thorac Cardiovasc Surg*. 2010;140:715-7.
- Petronio AS, De Carlo M, Bedogni F, Marzocchi A, Klugmann S, Maisano F, et al. Safety and efficacy of the subclavian approach for transcatheter aortic valve implantation with the CoreValve revalving system. *Circ Cardiovasc Interv*. 2010;3:359-66.
- Kappetein AP, Head SJ, Genereux P, Piazza N, van Mieghem NM, Blackstone EH, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *J Am Coll Cardiol*. 2012;60:1438-54.
- Ng ACT, Yiu KH, Ewe SH, Van Der Kleij, Bertini M, De Weger A, et al. Influence of left ventricular geometry and function on aortic annular dimensions as assessed with multi-detector row computed tomography: Implications for transcatheter aortic valve implantation. *Eur Heart J*. 2011;32:2806-13.
- Fraccaro C, Al-Lamee R, Tarantini G, Maisano F, Napodano M, Montorfano M, et al. Transcatheter aortic valve implantation in patients with severe left ventricular dysfunction: immediate and mid-term results, a multicenter study. *Circ Cardiovasc Interv*. 2012;5:253-60.
- Gilard M, Eltchaninoff H, Iung B, Donzeau-Gogue P, Chevreul K, Fajadet J, et al. Registry of transcatheter aortic-valve implantation in high-risk patients. *N Engl J Med*. 2012;366:1705-15.
- Tamburino C, Capodanno D, Ramondo A, Petronio AS, Etori F, Santoro G, et al. Incidence and predictors of early and late mortality after transcatheter aortic valve implantation in 663 patients with severe aortic stenosis. *Circulation*. 2011;123:299-308.
- Di Mario C, Eltchaninoff H, Moat N, Goicolea J, Ussia GE, Kala P, et al. The 2011-12 pilot European Sentinel Registry of Transcatheter Aortic Valve Implantation: in-hospital results in 4,571 patients. *EuroIntervention*. 2013;8:1362-71.
- Ussia GP, Barbanti M, Ramondo A, Petronio AS, Etori F, Santoro G, et al. The valve-in-valve technique for treatment of aortic bioprosthesis malposition: an analysis of incidence and 1-year clinical outcomes from the Italian CoreValve registry. *J Am Coll Cardiol*. 2011;57:1062-8.
- Ussia GP, Barbanti M, Sarkar K, Aruta P, Scarabelli M, Cammalleri V, et al. Transcatheter aortic bioprosthesis dislocation: technical aspects and midterm follow-up. *EuroIntervention*. 2012;7:1285-92.
- Geisbusch S, Bleiziffer S, Mazzitelli D, Ruge H, Bauernschmitt R, Lange R. Incidence and management of corevalve dislocation during transcatheter aortic valve implantation. *Circ Cardiovasc Interv*. 2010;3:531-6.
- Grube E, Naber C, Abizaid A, Sousa E, Mendiz O, Lemos P, et al. Feasibility of transcatheter aortic valve implantation without balloon pre-dilation: a pilot study. *JACC Cardiovasc Interv*. 2011;4:751-7.
- Lerakis S, Hayek SS, Douglas PS. Paravalvular aortic leak after transcatheter aortic valve replacement: current knowledge. *Circulation*. 2013;127:397-407.
- Khatri PJ, Webb JG, Rodes-Cabau J, Fremes SE, Ruel M, Lau K, et al. Adverse effects associated with transcatheter aortic valve implantation: a meta-analysis of contemporary studies. *Ann Intern Med*. 2013;158:35-46.
- Piazza N, Onuma Y, Jessurun E, Kint PP, Maugenes AM, Anderson RH, et al. Early and persistent intraventricular conduction abnormalities and requirements for pacemaking after percutaneous replacement of the aortic valve. *JACC Cardiovasc Interv*. 2008;1:310-6.
- Samim M, Stella PR, Agostoni P, Kluin J, Ramjankhan F, Sieswerda G, et al. Transcatheter aortic implantation of the Edwards-SAPIEN bioprosthesis: insights on early benefit of TAVI on mitral regurgitation. *Int J Cardiol*. 2011;152:124-6.

SUPPLEMENTARY METHODS

This supplementary methods section provides additional information on the methodology used in the 31-mm Medtronic CoreValve (MCV31) registry, discussing patient work-up, device characteristics, transcatheter implantation procedures, and statistical analysis.

Study Design

The study is an observational retrospective multicenter single-arm registry. All patients who underwent TAVI for severe aortic valve disease using the MCV31 device were retrospectively identified. Patients selected for TAVI had been considered unsuitable for SAVR by consensus of a cardiologist and cardiac surgeon, either because of a high predicted operative mortality risk (logistic EuroSCORE >15) or the presence of absolute contraindications for SAVR (eg, porcelain aorta). Further details on patient selection have been published previously.^{E1}

Pre-, intra-, and postprocedural data were retrospectively collected and documented in a registry. All patients gave informed consent for the procedure and because of the retrospective nature of the study design, ethics committee approval was waived.

Patient Evaluation

The evaluation of eligibility for TAVI included transthoracic echocardiography (TTE), transesophageal echocardiography (TEE), coronary angiography, and thoracoabdominal multislice computed tomography (MSCT). TTE was performed in all patients before TAVI and after the procedure before discharge. Left ventricular, valvular, and prosthesis function were evaluated by local experienced echocardiographers in compliance with dedicated guidelines.^{E2,E3} TEE could be also be performed, according to the routine of each participating center, to analyze concomitant mitral valve disease and measure the aortic annulus diameter. MSCT imaging was used to assess the suitability of vascular entrance sites, as well as to determine aortic annulus dimensions.

Prosthesis sizing was based on MSCT-derived aortic annulus measurements in most patients; in some cases, only TEE measurements were available. The reliability of these particular measurements and their compliance with findings from other imaging modalities were considered with close scrutiny by the interventional teams.

Device

The MCV31 device received CE (Conformité Européenne) approval in August 2011 for transfemoral, transaxillary and direct aortic implantation. It is currently the only valve prosthesis available for transcatheter treatment of patients with an aortic annulus diameter greater than 27 mm. The MCV31 has roughly the same design characteristic design as its smaller 26-mm and 29-mm predecessors.^{E4} It consists of a trileaflet porcine pericardial valve sutured into a nitinol frame. The frame has diamond-shaped cells with an hourglass-like architecture, in which 3 distinct regions of radial force can be identified. The outflow portion has low radial force and is designed to stabilize and center the device in the ascending aorta. The center portion contains the porcine leaflets and is therefore constrained to avoid obstruction of the coronary arteries. The inflow portion has high radial force to exclude the calcified leaflets and maintain intra-annular anchoring, and is covered with a pericardial skirt to minimize paravalvular aortic regurgitation (AR) after implantation. It is only this inflow portion that is actually larger in the 31-mm prosthesis compared with the 29-mm prosthesis (see article Figure 1), giving rise to a pronounced tapering of the inflow portion. Therefore, correct placement, high enough to allow proper apposition of the enlarged inflow part to the native aortic valve, is more critical than with the smaller sizes. The MCV31 is deployed using an 18-French delivery catheter with an AccuTrak stability layer (Medtronic Inc, Minneapolis, Minn).

TAVI

The TAVI procedures were performed via a transfemoral, transaxillary, or direct aortic approach according to the choice of the operators, using standard access techniques, under general anesthesia or conscious sedation. Technical details of the applied approaches have been discussed in detail elsewhere.^{E5,E6}

Predilatation of the native aortic valve was left to operator discretion and preferably performed to facilitate prosthesis implantation. Motivations for omitting predilatation were poor left ventricular function and mixed disease with an important regurgitation component. Prosthesis deployment was performed under fluoroscopic guidance. The use of stabilizing ventricular pacing (100-120 beats per minute) during deployment was at the discretion of the operator.

After implantation, aortography was used to assess valvular location and function as well as patency of the left and right coronary ostia. Valvular function was thereafter examined by echocardiography (either TTE, TEE, or intracardiac echocardiography), before the patient left the operating room.

End Point Definitions

In-hospital complications were registered in concordance with the recently published Valve Academic Research Consortium-2 (VARC-2) consensus document.^{E7} In compliance with the VARC-2 definitions, device success was defined as the proper implantation of the first valve prosthesis used, with intended performance of the prosthetic heart valve (peak aortic flow velocity <3 m/s and no moderate or severe AR) and no procedural mortality (30-day all-cause mortality).^{E7} In addition, acute procedural success was defined by the authors as the successful implantation of a single valve with proper functioning (correct anatomic position of the valve with no moderate or severe AR present) and the patient leaving the operating room alive.

Statistical Analysis

All data were analyzed using IBM SPSS Statistics software version 20 (IBM Corp., Armonk, NY). Results for continuous variables were presented as means $\pm$ standard deviation or medians [interquartile range], as considered appropriate. Categorical variables were reported as counts and percentages. Comparison of continuous variables was done using the Student *t* test for unpaired measures or the paired *t* test for repeated measures or their nonparametric equivalents, the Mann-Whitney *U* test and Wilcoxon signed ranks test, where appropriate. Categorical variables were analyzed using the χ^2 or Fisher exact test.

E-References

- E1. Holmes DR Jr, Mack MJ, Kaul S, Agnihotri A, Alexander KP, Bailey SR, et al. 2012 ACCF/AATS/SCAI/STS expert consensus document on transcatheter aortic valve replacement. *J Am Coll Cardiol*. 2012;59:1200-54.
- E2. Baumgartner H, Hung J, Bermejo J, Chambers JB, Evangelista A, Griffin BP, et al. Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. *Eur J Echocardiogr*. 2009;10:1-25.
- E3. Kappetein AP, Head SJ, Genereux P, Piazza N, van Mieghem NM, Blackstone EH, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *J Am Coll Cardiol*. 2012;60:1438-54.
- E4. Grube E, Buellesfeld L, Mueller R, Sauren B, Zickmann B, Nair D, et al. Progress and current status of percutaneous aortic valve replacement: results of three device generations of the CoreValve Revalving system. *Circ Cardiovasc Interv*. 2008;1:167-75.
- E5. Bruschi G, De Marco F, Fratto P, Oreglia J, Colombo P, Paino R, et al. Direct aortic access through right minithoracotomy for implantation of self-expanding aortic bioprosthetic valves. *J Thorac Cardiovasc Surg*. 2010;140:715-7.
- E6. Petronio AS, De Carlo M, Bedogni F, Marzocchi A, Klugmann S, Maisano F, et al. Safety and efficacy of the subclavian approach for transcatheter aortic valve implantation with the CoreValve revalving system. *Circ Cardiovasc Interv*. 2010;3:359-66.