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Original Article

Comparison of balloon-expandable valves versus self-expandable valves in high-risk patients undergoing transcatheter aortic valve replacement for severe aortic stenosis

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Abstract

Background: Transcatheter aortic valve implantation (TAVI) has emerged as an alternative to surgical aortic valve replacement for patients with symptomatic severe aortic stenosis (AS) who have a high surgical risk. In Taiwan, this is the first study reporting TAVI outcomes at a single center offering two different transcatheter heart valve technologies via four types of approaches. Our aim was to compare 30-day and 6-month Valve Academic Research Consortium-2 (VARC-2) outcomes of the two valves.

Methods: We reported the procedural, 30-day, and 6-month VARC-2 outcomes of high-risk patients who were consecutively treated with the Medtronic CoreValve (MCV) or with the Edwards SAPIEN valve or SAPIEN XT valve (ESV; Edwards Lifesciences, Irvine, CA, USA) delivered via four types of approaches.

Results: From May 2010 to December 2013, 30 consecutive patients with severe AS underwent TAVI: 15 patients were treated with the MCV and 15 patients were treated with the ESV. The transfemoral approach was the most frequently used route (13 MCV and 6 ESV), followed by the transapical approach (9 ESV), trans-subclavian approach (1 MCV), and direct aortic approach (1 MCV). There were no procedural deaths. "Device success" was achieved in 29 (96.7%) patients, and is defined as the absence of procedural mortality, correct positioning of one prosthetic heart valve into the proper anatomical location, and intended performance of the heart valve without moderate or severe regurgitation. The VARC-2–defined combined safety endpoint at 30 days was comparable between patients treated with the ESV and the MCV (33.3% vs. 20%, respectively; group, $p = 0.409$). At the 6-month follow up, the combined efficacy endpoint was not significantly different between the two groups (13.3% in the ESV group vs. 20% in the MCV group; $p = 0.624$). There was only one (3.3%) patient who required permanent pacemaker implantation.

Conclusion: For the first time in Taiwan, we have demonstrated that TAVI using either device is complementary and feasible for treating a wide range of patients by using a careful selection of approaches. Favorable overall procedural success rates and 30-day and 6-month outcomes were achieved with both devices.

Keywords: aortic stenosis; Edwards SAPIEN XT; Medtronic CoreValve; transcatheter aortic valve implantation

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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1. Introduction

Degenerative aortic stenosis (AS) is the most common valvular heart disease in adults. Its prevalence is approximately 4% in patients older than 80 years. After the onset of symptoms (e.g., angina, syncope, or heart failure), the average survival time is 2−3 years with a high risk of sudden death.[1] Surgical aortic valve replacement (AVR), which has been the only effective treatment in adults with severe symptomatic AS, provides symptomatic relief and long-term survival.[2] However, in clinical practice, > 30% of patients with severe symptomatic AS do not undergo AVR because of advanced age, left ventricular dysfunction, or the presence of multiple coexisting conditions.[3−6]

Transcatheter aortic valve implantation (TAVI) is a new procedure in which a bioprosthetic valve is inserted through a catheter and implanted within the diseased native aortic valve. In 2002, the procedure was first performed.[7] Since then, this technology has evolved tremendously and has become an established therapy in the treatment of symptomatic severe AS in patients deemed at too high a risk for surgical AVR.[8−15]

Two devices have been in widespread use: the self-expandable Medtronic CoreValve (MCV; Medtronic, Minneapolis, MN, USA) and balloon-expandable Edwards SAPIEN or SAPIEN XT valve (ESV; Edwards Lifesciences, Irvine, CA, USA). The MCV is a nitinol self-expandable porcine pericardial tissue valve. The ESV was initially composed of stainless steel (SAPIEN), but now composed of a cobalt chromium frame (SAPIEN XT) with bovine pericardial leaflets. Both valves reportedly have excellent flow characteristics, but each has specific features and aortic anatomic requirements.

In Taiwan, our multidisciplinary team was the first to apply to the Department of Health (DOH; Taipei, Taiwan) for approval of the TAVI program using the Edwards SAPIEN valve. In January 2010, the TAVI program was approved by the DOH. Ten patients with symptomatic severe AS, who were evaluated by surgeons as having a high surgical risk, underwent TAVI in our hospital.[16,17] In December 2013, the Ministry of Health and Welfare (Taipei, Taiwan) granted approval of the MCV. Since then, the MCV has been predominantly used in our center, except for patients who did not meet the anatomical criteria required for MCV implantation. Transcatheter aortic valve implantation was performed with the Edwards SAPIEN XT device for patients who were unsuitable for MCV.

To date, our institution offers two different transcatheter heart valve technologies in Taiwan. The aim of this single-center study was to compare 30-day and 6-month Valve Academic Research Consortium-2 (VARC-2)[18] outcomes after TAVI with ESV versus with MCV.

2. Methods

2.1. Patients

From May 2010 to December 2013 at our center, 30 consecutive patients underwent TAVI who had severe AS (i.e., valve area $\leq$ 1.0 cm^2 and mean aortic valve gradient $\geq$ 40 mmHg). All patients had New York Heart Association (NYHA) symptoms greater than Class II. Patients were selected for TAVI when they were considered unsuitable or at high risk for surgical AVR by the heart team discussion. Operative risk was calculated using the logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) score and the Society of Thoracic Surgeons predictive risk for mortality score. Patients at high surgical risk had a logistic EuroSCORE $\geq$ 20%; significant comorbidities; or other risk factors such as a porcelain aorta, previous chest radiation, the presence of patent coronary artery bypass grafts, liver cirrhosis, and frailty. Patients for whom TAVI was deemed as the best treatment option were selected based on the clinical consensus of a multidisciplinary team consisting of cardiac surgeons, interventional cardiologists, anesthetists, and imaging specialists.

The main exclusion criteria were a native aortic valve annulus of < 18 mm or > 29 mm, an acute myocardial infarction of < 14 days, a left ventricular ejection fraction of < 20%, active infection, hemodynamic instability, or a life expectancy of < 12 months.

2.2. Devices

In our practice, we initially performed TAVI with the Edwards SAPIEN valve (in 10 patients) in 2010. We then added the MCV to our practice after it was approved in December 2013. The MCV system has been predominantly used since then in our center. For patients unsuitable for MCV implantation (such as patients with shallow coronary sinuses or a dilated ascending aorta), TAVI was performed with the Edwards SAPIEN XT device.

2.3. MCV suitability

The annular dimension requirements for MCV are 20−23 mm for the 26-mm device, 23−27 mm for the 29-mm device, and 26−29 mm for the 31-mm device.[9] For transfemoral access, the device requires an 18-F delivery system and thus a minimal iliofemoral dimension of at least 6 mm. Adequate sinus of Valsalva width (> 27 mm for the 26-mm valve, and > 29 mm for the 29-mm and 31-mm valves) is also required. The ascending aortic diameter 40 mm distal to the aortic annulus should be < 40 mm for the 26-mm valve and < 43 mm for the 29-mm and 31-mm valves.

2.4. Edwards suitability

The annular dimension criteria for the Edwards SAPIEN device or SAPIEN XT device is 18−21 mm for the 23-mm device, 22−25 mm for the 26-mm device, and 25−27 mm for the 29-mm device.[19] The transfemoral access requirements for the Edwards SAPIEN valve with the RetroFlex 3 System (Edwards Lifesciences) is a minimal iliofemoral dimension of 7 mm for the 22-F/23-mm device, and a minimal iliofemoral dimension of 8 mm for the 24-F/26-mm device. The next-generation Edwards system (Edwards SAPIEN XT, USA)

with the Novaflex delivery system (Edwards Lifesciences) introduces the Edwards expandable sheath (i.e., e-sheath), available in sizes of 16-F and 18-F for the 23-mm and 26-mm devices, respectively. The criteria for feasibility include a minimal iliofemoral dimension of 6 mm for the 23-mm valve and a minimal iliofemoral dimension of 6.5 mm for the 26-mm valve.

2.5. Procedures

Depending on the patient's clinical conditions and the anesthesiologist's evaluation of the patient, the procedure was performed under general anesthesia or under local anesthesia with conscious sedation. The transapical procedures were all performed under general anesthesia. The standard approach for both valves was through the transfemoral route, if feasible. In patients who did not have the adequate anatomy to allow a safe transfemoral access, alternative access routes were used such as the transapical access[20] for the ESV, and the trans-subclavian access[21] or direct aortic access[22] for the MCV. Adjunctive pharmacologic therapy included administering heparin during the procedure, aspirin (100 mg/d) indefinitely, and clopidogrel (75 mg/d) for 3−6 months after the procedure.

2.5.1. Transfemoral approach

Transfemoral procedures were performed by the surgical cutdown of the femoral arteries or by the double-ProGlide (Abbott Vascular, Redwood, CA, USA) preclose technique.[23] After retrograde predilation of the native valve, the valve was crossed and implanted, as previously described.[8]

2.5.2. Transapical approach

For the transapical procedure, a left anterolateral mini-thoracotomy and pericardiotomy were performed. A double-pledgeted purse-string suture or U stitches were placed at the left ventricular apex. After puncturing the apex and performing antegrade crossing and predilation, the ESV was deployed under rapid ventricular pacing, as previously reported.[20]

2.5.3. Trans-subclavian approach

This procedure required surgical isolation of the left axillary artery. Once the artery was isolated, a purse-string suture was placed to allow subsequent closure at the end of the procedure. The artery was punctured at the distal end of the purse string, and a 6-F sheath was placed into the artery. A standard 0.035-inch guide wire was then exchanged for a preshaped 0.035-inch Amplatz Super Stiff guide wire (Boston Scientific, Marlborough, MA, USA), and an 18-F sheath was positioned in the axillary artery. The valve was crossed with the same procedure previously described for the transfemoral approach.[8] The axillary access site was then surgically repaired.[21]

2.5.4. Direct aortic approach

The procedure was performed through a 5-cm incision in the right second intercostal space. A right anterior mini-thoracotomy was formed so that the medial angle of incision was positioned just before the projection of the right internal mammary artery 1.5−2 cm lateral to the sternal edge. Basal ascending aorta aortography, using a graduated pigtail, was performed to measure the distance between the aortic annulus and the selected entry site in the ascending aorta. More than 6 cm were needed to safely perform MCV implantation. At the entry site, two aortic purse-string sutures for direct aortic access were placed in a standard fashion, as previously reported.[22]

2.6. Study endpoints

All clinical endpoints of this study were defined according to the VARC-2 criteria.[18] "Device success" was defined as the absence of procedural mortality, correct positioning of a single prosthetic heart valve into the proper anatomical location, and intended performance of the prosthetic heart valve (i.e., no prosthesis−patient mismatch and a mean aortic valve gradient < 20 mmHg or peak velocity > 3 m/s, and no moderate or severe prosthetic valve regurgitation). After valve deployment, independent investigators assessed the patient's valve function using transthoracic echocardiography prior to discharge, at the 3-month follow up, and at the 6-month follow up. The 30-day-combined safety endpoint is a combined endpoint, defined by VARC-2 as a composite of all-cause mortality, major stroke, life-threatening or disabling bleeding, acute stage 2 or 3 kidney injury such as renal replacement therapy, major vascular complications, and a repeat procedure for valve-related dysfunction. The VARC-2 proposed using the Acute Kidney Injury Network (AKIN) system for reporting acute kidney injury (AKI). "Acute kidney injury" was defined as an absolute (i.e., < 48 hours) reduction in kidney function and classified as stage 1 for a 150−199% increase in the serum creatinine level (i.e., 1.5−1.99 $\times$ the amount of increase from the baseline), or an increase in the creatinine level of > 0.3 mg/dL, or a urine output of < 0.5 mL/kg/h for > 6 hours but < 12 hours; as stage 2 for a 200−299% increase in the serum creatinine level (i.e., 2.0−2.9 $\times$ the amount of increase from the baseline level) or a urine output of < 0.5 mL/kg/h for > 12 hours but < 24 hours; and as stage 3 for an increase in serum creatinine level of $> 300\%$ (i.e., $> 3 \times$ the amount of increase from the baseline level) or a serum creatinine level of > 4.0 mg/dL with an acute increase of at least 0.5 mg/dL, or a new need for renal replacement therapy post-TAVI. The combined efficacy endpoint was defined as a composite of all-cause mortality, stroke, requirement of hospitalization for worsening heart failure, and valve-related dysfunction.

2.7. Statistical analysis

Continuous variables were expressed as the mean $\pm$ the standard deviation, and were analyzed with the Student t test or Wilcoxon rank sum test, depending on the variable distribution. Categorical variables were compared with the Chi-square test using Yates' correction for continuity or the Fisher's exact test. For all comparisons, $p < 0.05$ was considered statistically significant.

3. Results

3.1. Baseline characteristics

Between May 2010 and December 2013, 30 consecutive patients undergoing TAVI in our center were included in this analysis. The mean age was 81.3 ± 5.2 years, and all patients had severe symptomatic AS (i.e., mean aortic valve area, 0.61 cm^2; mean transaortic gradient, 50.1 ± 2.4 mmHg). Among these patients, two (6.7%) patients had a bicuspid aortic valve and two (6.7%) patients had previously undergone mitral valve replacement with a mechanical prosthesis. Table 1 shows the baseline clinical and echocardiographic characteristics of the study population. No significant differences were observed with respect to sex, body surface area, logistic EuroSCORE, NYHA class, aortic valve area, and mean pressure gradient between patients treated with ESV and patients treated with MCV. Compared to patients receiving the MCV, patients in the ESV group had a significantly lower baseline estimated glomerular filtration rate [GFR; 40.4 ± 16.3 mL/min (ESV) vs. 69.3 ± 25.8 mL/min (MCR); $p = 0.001$] and higher left ventricular ejection fraction (59.4 ± 8.0% vs. 50.9 ± 7.4%, respectively; $p = 0.006$).

Table 1
Baseline characteristics of the study population ($n = 30$).

Variable	Overall ($n = 30$)	ESV ($n = 15$)	MCV ($n = 15$)	p
Age (y)	81.3 ± 5.2	81.9 ± 2.6	80.7 ± 7.0	0.542
Men	14 (46.7)	7 (46.7)	7 (46.7)	> 0.99
Body mass index (kg/m^2)	23.0 ± 2.7	23.6 ± 2.9	22.5 ± 2.4	0.274
Body surface area (m^2)	1.56 ± 0.17	1.57 ± 0.15	1.55 ± 0.19	0.737
Hypertension	25 (83.3)	11 (73.3)	14 (93.3)	0.142
Diabetes mellitus	11 (36.7)	6 (40)	5 (33.3)	0.705
Hyperlipidemia	14 (46.7)	8 (53.3)	6 (40)	0.464
NYHA class III or IV	30 (100)	15 (100)	15 (100)	> 0.99
CAD	11 (36.7)	4 (26.7)	7 (46.7)	0.256
Previous MI	1 (3.3)	1 (6.7)	0	0.309
Previous PCI	10 (33.3)	4 (26.7)	6 (40)	0.439
Previous CABG	2 (6.7)	0	2 (13.3)	0.143
Peripheral artery disease	4 (13.3)	2 (13.3)	2 (13.3)	> 0.99
Cerebrovascular disease	7 (23.3)	4 (26.7)	3 (20)	0.666
Pulmonary disease	16 (53.3)	8 (53.3)	8 (53.3)	> 0.99
Previous BAV	8 (26.7)	3 (20)	5 (33.3)	0.409
Previous pacemaker	0	0	0	> 0.99
Logistic EuroSCORE (%)	25.1 ± 11.2	25.8 ± 11.8	24.4 ± 10.9	0.742
Serum creatinine (mg/dL)	1.1 ± 0.5	1.3 ± 0.6	1.0 ± 0.3	0.055
Estimated GFR (mL/min)	54.8 ± 25.8	40.4 ± 16.3	69.3 ± 25.8	0.001
Estimated GFR (<60 mL/min)	17 (56.7)	13 (86.7)	4 (26.7)	0.001
Bicuspid valve	2 (6.7)	2 (13.3)	0	0.143
Previous mitral prosthesis	2 (6.7)	1 (6.7)	1 (6.7)	> 0.99
Neoplasm	3 (10)	1 (6.7)	2 (13.3)	0.543
Echocardiographic findings				
Aortic valve area (cm^2)	0.61 ± 0.17	0.58 ± 0.18	0.64 ± 0.17	0.377
Mean PG (mmHg)	50.1 ± 20.4	49.6 ± 16.8	50.7 ± 24.1	0.881
LVEF (%)	55.1 ± 8.7	59.4 ± 8.0	50.9 ± 7.4	0.006
sPAP (>60 mmHg)	4 (13.3)	1 (6.7)	3 (20)	0.283

Data are presented as n (%) or mean ± the standard deviation.
BAV = balloon aortic valvuloplasty; CABG = coronary artery bypass grafting; CAD = coronary artery disease; ESV = Edwards SAPIEN or SAPIEN XT valve; GFR = glomerular filtration rate; Logistic EuroSCORE = Logistic European System for Cardiac Operative Risk Evaluation; LVEF = left ventricular ejection fraction; MCV = Medtronic CoreValve; MI = myocardial infarction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; PG = pressure gradient; sPAP = systolic pulmonary arterial pressure.

3.2. Procedural outcomes

Table 2 presents the main procedural variables. The transfemoral approach was the most frequently used route (63.3%), followed by the transapical approach (30%). The ESV device was implanted in 15 patients [in 6 (40%) patients via the transfemoral approach and in 9 (60%) patients via the transapical approach]. The MCV device was implanted in 15 patients [in 13 (86.7%) patients via the transfemoral approach, in 1 (6.7%) patient via the trans-subclavian approach, and in 1 (6.7%) patient via the direct aortic approach]. The transfemoral approach was less frequently used for the implantation of the ESV than for the MCV (40% vs. 86.7%, respectively; $p = 0.004$). Transcatheter aortic valve implantation was performed using local anesthesia in two (6.7%) patients in the MCV group. No significant difference was observed in the amount of contrast medium administered (212 ± 102 mL in the ESV group vs. 178 ± 84 mL in the MCV group; $p = 0.360$). The most

Table 2
The procedural characteristics and postprocedural outcomes of the study population ($n = 30$) at < 72 hours after the index procedure.

Variable	Overall ($n = 30$)	ESV ($n = 15$)	MCV ($n = 15$)	p
Bioprosthesis size				
ESV (23 mm)		6 (40)		
ESV (26 mm)		8 (53.3)		
ESV (29 mm)		1 (6.7)		
MCV (26 mm)			6 (40)	
MCV (29 mm)			9 (60)	
Access				0.004
Transfemoral	19 (63.3)	6 (40)	13 (86.7)	
Transapical	9 (30)	9 (60)	0	
Trans-subclavian	1 (3.3)	0	1 (6.7)	
Direct aortic	1 (3.3)	0	1 (6.7%)	
Contrast volume (mL)	192 ± 91	212 ± 102	178 ± 84	0.360
Local anesthesia	2 (6.7)	0	2 (13.3)	0.143
Device success [a]	29 (96.7)	14 (93.3)	15 (100)	0.309
Myocardial infarction	1 (3.3)	1 (6.7)	0	0.309
Stroke or TIA	1 (3.3)	0	1 (6.7) [b]	0.309
Acute kidney injury, stage 2 or 3	3 (10)	2 (13.3)	1 (6.7)	0.543
Major vascular complications	1 (3.3)	0	1 (6.7) [b]	0.309
New pacemaker implantation	1 (3.3)	1 (6.7)	0	0.309
Coronary obstruction	0	0	0	> 0.99
Cardiac tamponade	2 (6.7)	1 (6.7)	1 (6.7) [b]	> 0.99
Annulus rupture	0	0	0	> 0.99
Valve malpositioning	0	0	0	> 0.99
Need for a second valve	0	0	0	> 0.99
Posptocedural AR grade >2	1 (3.3)	1 (6.7)	0	0.309

Data are presented as n (%) or mean ± the standard deviation.
AR = aortic regurgitation; ESV = Edwards SAPEIN/SAPEIN XT valve; MCV = Medtronic CoreValve; TIA = transient ischemic attack.
[a] "Device success" is defined as the absence of procedural mortality, correct positioning of a single prosthetic heart valve into the proper anatomical location, and intended performance of the heart valve without moderate or severe regurgitation.
[b] All events occurred in one patient.

commonly used implant was the 26-mm valve (53.5%) in the ESV group and the 29-mm valve (60%) in the MCV group. Table 2 summarizes the procedural outcomes. Device success was achieved in 29 (96.7%) patients. One (3.3%) patient with bicuspid aortic valve and horizontal aorta in the ESV group had postprocedural moderate paravalvular regurgitation, as assessed by angiography and echocardiography. No procedural death occurred within the first 72 hours after TAVI. In the ESV group, one (3.3%) patient had periprocedural myocardial infarction. Acute kidney injury requiring temporary dialysis occurred in three (10%) patients: two patients in the ESV group and one MCV recipient. Two (6.7%) patients had cardiac tamponade (categorized as life-threatening bleeding, according to the VARC-2 definition). In the first patient, cardiac tamponade occurred immediately after the deployment of the 26-mm Edwards SAPIEN valve, and prompt pericardiocentesis successfully stabilized the patient. It may have resulted from an aortic tear caused by asymmetrical distribution of aortic annulus calcification. The second patient had a left ventricular perforation (defined as a major vascular complication by the VARC-2) caused by the Amplatz Superstiff wire soon after the implantation of a 29-mm CoreValve. Pericardiocentesis was insufficient; therefore, surgical closure was performed. This patient developed a stroke from hypovolemic shock. Only one (3.3%) patient with bicuspid aortic valve required a permanent pacemaker after the implantation of a 29-mm Edwards SAPIEN XT valve. Proper device positioning was achieved in all patients, and no patient needed a second valve.

3.3. The VARC-2 outcome at 30 days and 6 months

Table 3 summarizes the 30-day and 6-month outcomes. At the 30-day follow up, no cardiovascular death had occurred. One patient in the ESV group died 25 days after the transapical procedure because of pneumonia and subsequent sepsis. Stage 3 AKI developed in two (6.7%) patients after 72 hours: one patient in the ESV group and one patient in the MCV group. The *cumulative incidence* of stage 2 or 3 AKI at the 30-day follow up was 16.7% (5 patients); of these patients, three (10%) patients had to be dialyzed temporarily and one (3.3%) patient needed chronic renal replacement therapy. Patients who presented with AKI had a significantly lower baseline estimated GFR, compared to patients not experiencing postprocedural renal impairment (26.0 ± 10.8 mL/min vs. 60.6 ± 24.0 mL/min, respectively; $p = 0.003$) and a higher serum creatinine level (1.94 ± 0.71 mg/dL vs. 0.97 ± 0.29 mg/dL, respectively; $p = 0.035$). They also more frequently had a history of coronary artery disease (80% vs. 28%, respectively; $p = 0.033$) and tended to have a higher logistic EuroSCORE score (34.1 ± 10.0% vs. 23.3 ± 10.7%, respectively; $p = 0.053$). There was no association between AKI and hypertension, diabetes, echocardiographic parameters, or contrast medium volume. There was no coronary artery obstruction or valve-related dysfunction requiring a repeat procedure within 30 days. The VASC-2−defined combined safety endpoints at 30 days were consequently comparable between patients treated with ESV or with MCV (33.3% in the ESV group vs. 20% in the MCV group; $p = 0.409$).

Between 30 days and 6 months, three more patients died (1 patient in the ESV group and 2 patients in the MCV group), which resulted in a 6-month cumulative all-cause mortality rate of 13.3%. No death was cardiac-related. One patient in the ESV group who required chronic renal replacement therapy died at 147 days because of an intracranial hemorrhage after a fall. Another two patients in the MCV group died between 30 days and 6 months. Both developed AKI after the TAVI; one

Table 3
The VARC-2 outcomes at the 30-day and 6-month follow up.

Outcome	Overall ($n = 30$)	ESV ($n = 15$)	MCV ($n = 15$)	p
30 days				
All-cause mortality	1 (3.3)	1 (6.7)	0	0.309
Cardiac mortality	0	0	0	> 0.99
All stroke	1 (3.3)	0	1 (6.7)	0.309
Life-threatening bleeding	2 (6.7)	1 (6.7)	1 (6.7)	> 0.99
Acute kidney injury, stage 2 or 3	5 (16.7)	3 (20)	2 (13.3)	0.624
Coronary artery obstruction	0	0	0	> 0.99
Major vascular complication	1 (3.3)	0	1 (6.7)	0.309
Valve-related dysfunction requiring repeat procedure (BAV, TAVI, or SAVR)	0	0	0	> 0.99
Combined safety end point	8 (26.7)	5 (33.3)	3 (20)	0.409
6-month cumulative clinical outcomes				
All-cause mortality	4 (13.3)	2 (13.3)	2 (13.3)	> 0.99
Cardiac mortality	0	0	0	> 0.99
All stroke	1 (3.3)	0	1 (6.7)	0.309
Requiring hospitalizations for worsening heart failure	1 (3.3)	0	1 (6.7)	0.309
NYHA class III or IV	1 (3.3)	0	1 (6.7)	0.309
Valve-related dysfunction [a]	0	0	0	> 0.99
Combined efficacy	5 (16.7)	2 (13.3)	3 (20)	0.624

Data are presented as n (%) or mean ± the standard deviation.

BAV = balloon aortic valvuloplasty; ESV = Edwards SAPIEN or SAPIEN XT valve; MCV = Medtronic CoreValve; NYHA = New York Heart Association; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation; VARC = Valve Academic Research Consortium.

[a] "Valve-related dysfunction" refers to a mean aortic valve gradient > 20 mmHg, an effective orifice area <0.9−1.1 cm^2, and/or a Doppler velocity index of < 0.35 m/s, and/or moderate or severe prosthetic valve regurgitation.

patient needed rehospitalization for heart failure (NYHA Class IV) at 57 days and died of recurrent infection and multiorgan failure from sepsis at 98 days, and the other patient had repeated upper gastrointestinal bleeding and recurrent infection and died of sepsis at 179 days.

No valve-related dysfunction, which includes the presence of moderate or severe prosthesis regurgitation, was observed within 6 months. The VASC-2-defined combined efficacy endpoints at the 6-month follow up was accordingly the same in both groups (13.3%). At 6 months, the patients who experienced AKI had a higher all-cause mortality, compared to patients without AKI (60% vs. 3.6%, respectively), which remained statistically significant in the age and sex-adjusted Cox regression model (hazard ratio, 14.2; $p = 0.026$).

4. Discussion

In Taiwan, this is the first study reporting TAVI outcomes at a single center that offers two different transcatheter heart valve technologies via four different approaches in high-risk patients with severe AS. The overall device success rate of 96.7% is encouraging, and suggests that, with careful planning and appropriate technique, immediate procedural success can be achieved in most patients in whom the procedure is attempted.

Transcatheter aortic valve implantation has been very successfully used in the treatment of high-risk and inoperable patients with severe AS. The two devices in mainstream use are the MCV and the ESV. In December 2013, the Ministry of Health and Welfare (Taipei, Taiwan) granted approval of the self-expandable MCV. Since then, the device has been predominantly used in Taiwan. However, three (16.7%) of our 18 patients assessed by the Medtronic core lab were ineligible for treatment with the MCV system: two patients had shallow coronary sinuses and one patient had a severely angulated and dilated ascending aorta. Therefore, the use of either device is complementary and makes TAVI feasible for patients with a wide array of anatomic dimensions. In addition, using various access routes ensures that most patients can be treated.

In our cohort, the transfemoral approach was less frequently used for implanting the ESV than for implanting the MCV (40% vs. 86.7%, respectively; $p = 0.004$). Two-thirds of the ESVs were implanted in 2010, when only the earlier generation RetroFlex System (which requires the use of the larger diameter 22-F to 24-F sheath) was available; therefore, a comparison of the ESVs, which were mostly implanted via transapical approach, and the MCVs, which were mostly implanted via transfemoral approach, is unfair, to some extent. Alli et al[24] report that there was consistently a learning curve for TAVI and that at least 30 procedures were needed for procedural proficiency. We still achieved excellent results, despite being in the learning curve period.

Accumulating data have linked device failure and more-than-mild aortic regurgitation (AR) after TAVI with significantly increased long-term mortality after TAVI.[13,25] No patient in our series had valve embolization, ectopic valve deployment, the need for a valve-in-valve procedure, or conversion to surgery. Higher frequencies of postprocedural AR have been more recently reported for MCV than for ESV in a well-balanced cohort from the United Kingdom Transcatheter Aortic Valve Implantation (U.K. TAVI) registry (452 MCV patients vs. 410 ESV patients; moderate AR vs. severe AR, 17.3% vs. 9.6%, respectively; $p = 0.001$)[14] and in the large French Transcatheter Aortic Valve Intervention Registry (FRANCE-2) study [21.5% (MCV) vs. 13.9% (ESV)].[15] By contrast, in a recently published multicenter collaborative study—the Pooled-Rotterdam-Milano-Toulouse In Collaboration Plus (PRAGMATIC PLUS) Initiative—the incidence of more-than-mild AR was extremely low and comparable between both devices (2.0% with MCV and 1.8% with ESV).[26] In all of these studies, the AR was assessed by angiography (U.K. registries) or by echocardiography (FRANCE 2 and PRAGMATIC PLUS). In our institution, valve function after TAVI was assessed by independent investigators using transthoracic echocardiography prior to discharge, at the 3-month follow up, and at the 6-month follow up. There was only one (3.3%) patient with bicuspid aortic valve and horizontal aorta in the ESV group who experienced postprocedural moderate paravalvular regurgitation.

The MCV implantation is frequently associated with atrioventricular block that requires pacemaker placement. This is possibly because of greater expansion into the left ventricular outflow tract with compression of the septal conduction tissues. The need for permanent pacemaker placement after MCV implantation has accordingly been reported in 25.8–33.0% of patients.[27,28] In our study, the rate of permanent pacemaker requirement was only 3.3% (one patient in the ESV group with a bicuspid aortic valve received a 29-mm device), which is one of the lowest rates that has been observed so far.[27,28] That may result from our high implantation strategy for the MCV system at a target depth of $\leq$ 6 mm below the annulus. The strategy has to be validated in further studies to confirm whether it can abolish the high rate of permanent pacemaker requirement with MCV implantation.

Our results are encouraging overall, but the *incidence* of stage 3 AKI at 30 days was 16.7% (5 patients); of these, three (10%) patients had to be dialyzed temporarily and one (3.3%) patient needed chronic renal replacement therapy. The incidence of AKI in large analyses was 20–21%, and severe worsening of renal function (i.e., AKI stages 2 and 3) occurred in 5.3% of patients.[29,30] Transcatheter aortic valve implantation-related AKI was associated with increased 30-day, 6-month, and 1-year mortality.[31,32] In our series, patients who developed AKI had significantly lower baseline estimated GFR and higher serum creatinine level. No significant differences existed in the amount of contrast media administered. At 6 months, patients who experienced AKI had a higher all-cause mortality, compared to patients without AKI (60% vs. 3.3%, respectively; $p = 0.001$), which remained statistically significant in the age and sex-adjusted Cox regression model (hazard ratio, 14.2; $p = 0.026$).

The present study summarizes a rather small number of high-risk patients and encompasses the experience of a single center. Therefore, the generalizability of our findings may not

extend to all clinical centers performing TAVI. The present study was prospective, but the choice of treatment was not randomized. In addition, there may be a learning curve for the procedure and with regard to careful patient selection because of many risk factors and contraindications that are known to date and are better understood with increasing experience. In the present study, all patients were monitored by overseas proctors. Thus, the study outcomes may not reflect real-world scenarios. Further technical improvements of the technology will definitely lead to the evolution of smaller devices, which may rapidly increase the number of transfemoral procedures performed.

In conclusion, our data demonstrated that TAVI is a safe and effective procedure in selected extreme high-risk elderly patients with severe AS. With the current state of the art techniques, and various alternative approaches, TAVI can be applied in a wide range of patients.

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