Characteristics and outcomes following transcatheter aortic valve replacement in China: a report from China aortic valve transcatheter replacement registry (CARRY)

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Abstract

Background: The past decade has witnessed an ever-increasing momentum of transcatheter aortic valve replacement (TAVR) and a subsequent paradigm shift in the contemporary management of severe aortic stenosis (AS). We conducted a multi-centric TAVR registry based on Chinese patients (the China Aortic valve tRanscatheter Replacement registrY [CARRY]) to delineate the clinical characteristics and outcomes of Chinese patients who underwent TAVR and compare the results between different valve types in different Chinese regions.

Methods: CARRY is an all-comer registry of aortic valve disease patients undergoing TAVR across China and was designed as an observational study that retrospectively included all TAVR patients at each participating site. Seven hospitals in China participated in the CARRY, and 1204 patients from April 2012 to November 2020 were included. Categorical variables were compared using the chi-squared test, and continuous variables were analyzed using a *t* test or analysis of variance (ANOVA) test. The Kaplan–Meier curve was used to estimate the risk of adverse events during follow-up.

Results: The mean age of the patients was 73.8 ± 6.5 years and 57.2% were male. The median Society of Thoracic Surgeon-Predicted Risk of Mortality score was 6.0 (3.7–8.9). Regarding the aortic valve, the proportion of bicuspid aortic valve (BAV) was 48.5%. During the hospital stay, the stroke rate was 0.7%, and the incidence of high-degree atrioventricular block indicating permanent pacemaker implantation was 11.0%. The in-hospital all-cause mortality rate was 2.2%. After 1 year, the overall mortality rate was 4.5%. Compared to patients with tricuspid aortic valve (TAV), those with BAV had similar in-hospital complication rates, but a lower incidence of in-hospital mortality (1.4% *vs.* 3.3%) and 1 year mortality (2.3% *vs.* 5.8%).

Conclusions: TAVR candidates in China were younger, higher proportion of BAV, and had lower rates of post-procedural complications and mortality than other international all-comer registries. Given the use of early generation valves in the majority of the population, patients with BAV had similar rates of complications, but lower mortality than those with TAV. These findings further propel the extension of TAVR in low-risk patients.

Trial Registration: https://www.chictr.org.cn/ (No. ChiCTR2000038526).

Keywords: Aortic stenosis; Aortic valve; Transcatheter aortic valve replacement

Introduction

The past decade has witnessed an ever-increasing momentum of transcatheter aortic valve replacement (TAVR) and a subsequent paradigm shift in the contem- porary management of severe aortic stenosis (AS).[1-3] The safety and efficacy profile of TAVR across all risk strata in severe AS has been carefully examined and confirmed in several pivotal randomized clinical trials (RCTs) and landmark studies.[4,5] Device refinement, accumulating

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experience, imaging processing iteration, and the heart team approach have driven these important progresses.[6] However, pressing issues remain in the TAVR and post-TAVR era, such as a younger population with a higher incidence of the bicuspid aortic valve (BAV) as TAVR expands to low-risk patients, implant-associated complications, and long-term durability.[7] A real-world study provides a truer portrayal of these issues, as well as an insight for future RCT design.

Existing data show that TAVR prognosis differs by country and region, which is mainly driven by differences in clinical characteristics, including age, valve morphology, and implanted device. The average age of Chinese TAVR recipients is approximately five years younger than that of the developed countries.[8-10] Therefore, Chinese TAVR patients represent an ideal study population that, if analyzed properly, can provide a valuable insight into the TAVR expansion in younger and low-risk patients. China currently has more than 100 valve centers capable of performing TAVR; however, to the best of our knowledge, the characteristics and outcomes of Chinese patients have not been systemically reported before.

Thus, we conducted a multi-centric TAVR registry based on Chinese patients (ie, China Aortic valve tRanscatheter Replacement registrY [CARRY]) and aimed to delineate the clinical characteristics and outcomes of Chinese TAVR patients and compare the results between different valve types and different regions.

Methods

Ethical approval

The study was approved by the Ethics Committee of West China Hospital (Approval No. 2019–975) as the lead organizer of CARRY. The informed consent was exempted because of the retrospective purpose. The ethics committees of other participating centers filed this approval on record for reference to regulate the conduction of CARRY in corresponding institutions.

CARRY registry and population

CARRY is an all-comer registry of patients with aortic valve disease undergoing TAVR across China (No. ChiCTR2000038526) and was designed as an observational study that retrospectively included all TAVR patients at each participating site. The registry was initiated and approved in December 2019 and was opened to any willing and qualified TAVR centers.

Seven hospitals in China participated in the CARRY. Once entering the registry, the center started to retrospectively record all the TAVR procedures that had been done into the registry. A total of 1204 patients from April 2012 to November 2020 were included. All participating sites were trained, and data were collected through an electronic data capture system (EDC; eCollect system powered by Taimei Technology, version 1.4, Zhejiang, China). The de-identified data were then converted to a research institute with no relevant conflicts of interest.

All patients were grouped by the following in accordance with the research rationale.

By site and region: Northeast, Central-east, Central-south, Southwest, and Northwest based on the site location.

By aortic valve morphologies: BAV or tricuspid aortic valve (TAV).

Data collection

Multiple parameters were included in the database, including the following:

Baseline patient characteristics, including patient demographics, past medical history, pre-procedural status, lab tests, medication, and cardiovascular imaging studies; procedural data, including procedure type, surgical risk, vascular access, pre- and post-dilation, valve size and type, and intra-procedural hemodynamics; periprocedural complications, including cardiovascular adverse events, stroke, vascular complications, bleeding, and device-associated events; post-procedural data, including the lab test, serial electrocardiography, and echocardiography; hospitalization information, including length of stay, medication, New York Heart Association (NYHA) class at discharge, in-hospital outcomes; follow-up outcomes, including follow-up duration, location, cause and time of death (if applicable), echocardiography, medication, and other cardiovascular adverse events.

Data were retrieved and collected at each site using a site-exclusive account. TAVR recipient information was filled into the EDC system at each center and was verified monthly by the clinical research associate. All the data were sorted and verified by the data manager.

Statistical analysis

The primary endpoint was defined as the all-cause mortality at 1 year, and the secondary endpoint was the complications or adverse events that occurred during the procedure or follow-up. Continuous variables were expressed as mean ± standard deviation, whereas medians (Q1, Q3) were used in non-normally distributed variables. The categorical variables are expressed as percentages. Categorical variables were compared using chi-square statistics, and continuous variables were analyzed using t test or analysis of variance (ANOVA) statistics. The Kaplan-Meier curve was used to estimate the risk of adverse events during follow-up. Statistical significance was considered at a two-tailed $P < 0.05$. All computations were performed using Spyder (based on Python 3.7) and Stata 15.1 software (College Station, TX, StataCorp LLC, USA).[11]

Results

Baseline characteristics

By March 2021, a total of 1216 patients were registered in the EDC system of CARRY. Eight patients were excluded due to the excessive lack of data (including key endpoints).

Table 1: Baseline clinical characteristics for patients undergoing TAVR (by regions).

Characteristics	Total	Northeast	Northwest	Southwest	Central-south	Central-east	Statistical values	P values
Number of patients, n (%)	1204 (100.0)	120 (10.0)	19 (1.6)	889 (73.8)	82 (6.8)	94 (7.8)		
Baseline characteristics								
Age (year)	73.8 ± 6.5	73.9 ± 6.9	73.8 ± 6.2	73.8 ± 6.5	73.4 ± 4.6	74.1 ± 7.0	0.012*	1.000
Height (cm)	161.0 ± 8.2	164.1 ± 7.5	164.8 ± 11.2	159.8 ± 7.9	159.3 ± 8.5	166.0 ± 7.6	0.181*	0.948
Weight (kg)	59.5 ± 10.9	64.7 ± 10.6	70.1 ± 12.2	57.9 ± 9.9	55.8 ± 11.5	65.6 ± 11.7	0.425*	0.795
Sex								
Male	57.2 (569/994)	54.2 (65/120)	64.3 (9/14)	56.3 (385/684)	57.3 (47/82)	67.0 (63/94)	4.670†	0.322
NYHA functional class III-IV	79.7 (705/885)	50.0 (50/100)	41.7 (5/12)	84.5 (533/631)	73.0 (73/82)	51.2 (44/60)	19.313†	<0.001
Previous cardiac procedure								
Previous PCI	11.7 (118/1010)	12.5 (15/120)	14.3 (2/14)	11.3 (79/700)	12.2 (10/82)	12.8 (12/94)	0.386†	0.982
Previous CABG	1.6 (6/365)	1.7 (2/120)	0 (0/14)	1.8 (1/55)	0 (0/82)	3.2 (3/94)	3.099†	0.549
Previous PPMI	2.5 (25/1008)	1.7 (2/120)	0 (0/14)	2.7 (19/699)	0 (0/81)	4.3 (4/94)	3.839†	0.431
Prevous ICD	0.1 (1/1003)	0 (0/120)	0 (0/14)	0.1 (1/701)	0 (0/74)	0 (0/94)	0.025†	1.000
Previous comorbidity								
History of stroke	9.9 (29/293)	18.3 (22/120)	7.1 (1/14)	3.8 (2/53)	0 (0/12)	4.3 (4/94)	16.737†	0.002
History of TIA	0.7 (2/304)	0.8 (1/120)	0 (0/14)	1.9 (1/52)	0 (0/24)	0 (0/94)	2.297†	0.686
Hypertension	44.3 (430/971)	40.8 (49/120)	57.1 (8/14)	43.6 (288/661)	31.7 (26/82)	62.8 (59/94)	20.043†	<0.001
Diabetes mellitus	20.1 (195/970)	20.8 (25/120)	21.4 (3/14)	18.6 (123/660)	15.9 (13/82)	15.9 (15/94)	1.294†	0.864
Coronary artery disease	31.2 (302/967)	29.2 (35/120)	21.4 (3/14)	31.6 (208/658)	23.5 (19/81)	23.5 (22/94)	4.645†	0.326
Myocardial infarction	2.9 (27/946)	8.3 (10/120)	7.1 (1/14)	1.8 (12/658)	0 (0/60)	4.3 (4/94)	16.821†	0.002
Atrial fibrillation	16.4 (158/965)	19.5 (23/118)	0 (0/14)	17.4 (114/657)	12.2 (10/82)	11.7 (11/94)	16.994†	0.002
Conduction block	9.8 (74/756)	15.3 (18/118)	28.6 (4/14)	8.3 (37/448)	14.6 (12/82)	3.2 (3/94)	20.985†	<0.001
Chorionic obstructive pulmonary disease	32.6 (316/969)	1.7 (2/120)	7.1 (1/14)	44.9 (297/661)	11.3 (9/80)	7.4 (7/94)	19.657†	<0.001
Chorionic kidney disease	7.4 (72/967)	4.2 (5/120)	7.1 (1/14)	7.4 (49/660)	12.7 (10/79)	7.4 (7/94)	19.768†	<0.001
Creatinine (μmol/L)	94.8 ± 71.0	83.8 ± 33.0	83.6 ± 23.3	95.2 ± 53.8	NA	107.7 ± 163.1	0.413*	0.799
Peripheral arterial disease	26.0 (244/939)	3.3 (4/120)	0 (0/14)	36.2 (239/660)	0 (0/51)	1.1 (1/94)	29.082†	<0.001
Anti-coagulation drug	14.5 (98/678)	13.3 (16/120)	7.1 (1/14)	7.3 (27/371)	0 (0/79)	57.4 (54/94)	19.091†	<0.001
Anti-platelet drug	52.9 (413/780)	36.7 (44/120)	100.0 (14/14)	55.8 (264/473)	5.1 (4/79)	92.6 (87/94)	26.941†	<0.001
Cardiotonic drug	4.9 (30/610)	10.8 (13/120)	0 (0/14)	2.9 (11/380)	50.0 (1/2)	5.3 (5/94)	29.086†	<0.001
Morphology of aortic valve								
BAV	48.5 (507/1045)	61.1 (55/90)	94.1 (16/17)	45.9 (359/782)	58.0 (40/69)	42.5 (37/87)	19.570†	<0.001
TAV	51.5 (538/1045)	38.9 (35/90)	5.9 (1/17)	54.1 (423/782)	42.0 (29/69)	57.5 (50/87)	20.753†	<0.001

Data was presented as n (%) or mean ± SD or % (n/N). * F value. † Chi-square value. BAV: Bicuspid aortic valve; CABG: Coronary artery bypass grafting; ICD: Implantable cardioverter defibrillator; NA: Not available; NYHA: New York heart association; PCI: Percutaneous coronary intervention; PPMI: Permanent pacemaker implantation; TAV: Tricuspid aortic valve; TAVR: Transcatheter aortic valve replacement; TIA: Transient ischemic attacks.

Another four patients did not undergo TAVR and were excluded. A total of 1204 TAVR patients from April 2012 to November 2020 were included in the final analysis. The mean age was 73.8 ± 6.5 years and 57.2% (705/885) of patients were males. The mean Society of Thoracic Surgeon-Predicted Risk of Mortality score was 6.0 (3.7–8.9) and 42.4% (323/745) of the patients had a score of 8 or higher. Among the total population, 79.7% (705/885) were classified under the NYHA class III-IV. Patient characteristics according to the region are shown in Table 1. For all patients with valve morphology data, the proportions of BAV (48.5%, $n = 507$) and TAV (51.5%, $n = 538$) were similar. There was no statistically significant difference in the average age between the two groups ($P = 0.335$). The prevalence of bicuspid anatomy in each age tertile is as follows: < 50: 100.0%, 50–60: 77.8%, 60–70: 51.2%, 70–80: 50.8%, 80–90: 36.6%, and 90–100: 57.1%. The patient characteristics according to valve morphology are detailed in Supplementary Table 1, http://links.lww.com/CM9/A847.

Procedural characteristics

Among all patients, 56.3% (566/1005) underwent TAVR under general anesthesia. Transfemoral access was chosen in 99.2% (1192/1202) of the patients. Balloon pre-dilation was performed in 88.4% (771/872) of cases, and this proportion was highest in the central south, reaching 100% (82/82). Valve-in-valves were performed in 5.3% (64/1202) of the patients. Procedural data are summarized in Table 2.

Echocardiography characteristics

Based on echocardiography assessment, TAVR significantly improved the patient's hemodynamics. The mean pre- and post-procedural left ventricular ejection fraction were 53.3 ± 14.1% and 55.8 ± 11.8%, respectively ($P < 0.001$). The average aortic valve (AVA) area was 0.7 (0.3–1.5) cm^2 before the procedure and 1.6 (1.4–2.2) cm^2 after TAVR ($P < 0.001$). The pre- and post-TAVR maximum velocity (V_{max}) were 4.8 ± 0.9, and 2.3 ± 0.6 m/s, respectively ($P < 0.001$). The mean pressure gradient (MPG) was 57.6 ± 21.8 mmHg before the procedure and 13.0 ± 6.4 mmHg after TAVR ($P < 0.001$). The echocardiographic characteristics are detailed in Table 3.

Complications during hospitalization

During the hospital stay, the stroke rate was 0.7% (9/1204); the incidence of high-degree atrioventricular block indicating permanent pacemaker implantation (PPMI) was 11.0% (133/1204); and coronary obstruction occurred in 0.6% (7/1204). The incidence of these adverse events

Table 2: Procedural characteristics for patients undergoing TAVR (by regions).

Characteristics	Total	Northeast	Northwest	Southwest	Central-south	Central-east	Statistical values (Chi-square value)	P values
Number of patients, n (%)	1204 (100.0)	120 (10.0)	19 (1.6)	889 (73.8)	82 (6.8)	94 (7.8)		
Anesthesia								
General anesthesia	56.3 (566/1005)	100.0 (120/120)	100.0 (14/14)	37.2 (259/697)	100.0 (81/81)	98.9 (92/93)	26.071	<0.001
Conscious sedation	43.7 (439/1005)	0 (0/120)	0 (0/14)	62.8 (438/697)	0 (0/81)	1.1 (1/93)	39.463	<0.001
Access								
Trans-femoral artery (Percutaneous)	94.0 (1130/1202)	92.5 (111/120)	100.0 (19/19)	93.5 (830/888)	100.0 (81/81)	94.7 (89/94)	7.406	0.116
Trans-femoral artery (Surgical)	5.2 (63/1202)	6.7 (8/120)	0 (0/19)	6.1 (54/888)	0 (0/81)	1.1 (1/94)	10.501	0.032
Trans-apical route	0.4 (5/1202)	0.8 (1/120)	0 (0/19)	0 (0/888)	0 (0/81)	4.3 (4/94)	19.073	<0.001
Trans-carotid artery	0.2 (2/1202)	0 (0/120)	0 (0/19)	0.2 (2/888)	0 (0/81)	0 (0/94)	0.712	0.950
Trans-axillary artery	0.2 (2/1202)	0 (0/120)	0 (0/19)	0.2 (2/888)	0 (0/81)	0 (0/94)	0.712	0.950
Balloon pre-expansion	88.4 (771/872)	94.2 (113/120)	100.0 (14/14)	87.6 (493/563)	100.0 (82/82)	74.2 (69/93)	19.056	<0.001
Implantation success (1st time)	98.2 (833/848)	96.7 (116/120)	100.0 (14/14)	98.5 (533/541)	98.8 (79/80)	97.8 (91/93)	2.409	0.661

Data was presented as n (%) or % (n/N). TAVR: Transcatheter aortic valve replacement.

Table 3: Peri-procedural echocardiographic data for patients undergoing TAVR.

Data	Total	Northeast	Northwest	Southwest	Central-south	Central-east	t values	P values (between pre-TAVR and post-TAVR)
Number of patients, n (%)	1204 (100.0)	120 (10.0)	19 (1.6)	889 (73.8)	82 (6.8)	94 (7.8)		
LVEF (%)							4.067	<0.001
Pre-TAVR	53.3 ± 14.1	51.4 ± 12.2	52.2 ± 14.4	54.9 ± 14.5	46.6 ± 13.3	50.7 ± 11.4		
Post-TAVR	55.8 ± 11.8	54.4 ± 8.5	53.6 ± 8.1	56.6 ± 12.2	50.8 ± 12.5	53.7 ± 10.5		
AVA (cm^2)							3.758	<0.001
Pre-TAVR	0.7 (0.3–1.5)	0.6 (0.4–0.8)	0.3 (0.2–0.4)	0.3 (0.2–0.4)	NA	1.8 (0.5–2.7)		
Post-TAVR	1.6 (1.4–2.2)	1.7 (1.4–2.1)	1.8 (1.7–1.8)	NA	NA	4.5 (4.4–4.6)		
Vmax (m/s)							5.631	<0.001
Pre-TAVR	4.8 ± 0.9	4.8 ± 0.8	5.0 ± 0.9	4.8 ± 0.9	5.1 ± 0.8	4.5 ± 1.1		
Post-TAVR	2.3 ± 0.6	2.3 ± 0.5	2.0 ± 0.3	2.4 ± 0.6	2.4 ± 0.5	2.5 ± 0.6		
MPG (mmHg)							19.204	<0.001
Pre-TAVR	57.6 ± 21.8	55.9 ± 21.7	70.8 ± 29.6	58.6 ± 20.7	54.9 ± 20.0	54.3 ± 29.9		
Post-TAVR	13.0 ± 6.4	11.3 ± 5.7	12.2 ± 6.4	13.2 ± 6.6	13.2 ± 5.5	14.0 ± 6.1		

AVA: Aortic valve area; LVEF: Left ventricular ejection fraction; MPG: Mean pressure gradient; NA: Not available; TAVR: Transcatheter aortic valve replacement; Vmax: Maximum velocity.

between regions did not appear to be statistically significant. The incidence of new-onset atrial fibrillation was 0.6% (7/1204), which was the highest in the Northeast region (3.3% [4/120]). Major vascular complications occurred in 1.1% (13/1204) of the cases and were highest in the central south region (6.1% [5/82]) and lowest in the northeast, northwest, and eastern regions (all 0%) [Table 4].

Mortality and follow-up

The all-cause mortality was 2.2% (26/1204) during the hospital stay, which was the highest in the central south (6.1% [5/82]), 4.3% (4/94) in the eastern region, 0% (0/19) in the northwest region, 1.8% (16/889) in the southwest region, and 0.8% (1/120) in the northeast region ($P = 0.042$). The 30-day mortality rate was 2.3% (27/1204). The in-hospital mortality was comparable with the 30-day mortality, possibly due to the long stay of high-risk patients. The 1-year, 3-year, and 5-year follow-ups were completed in 82.1%, 45.1%, and 30.2% of the patients, respectively. The cumulative 1-year mortality rate was 4.5%, and the Kaplan-Meier curve for each region is shown in Figure 1 (log rank $P = 0.157$).

Outcomes comparison between bicuspid and tricuspid

Compared to patients with TAV, those with BAV had a higher rate of general anesthesia (65.0% vs. 49.1%, $P < 0.001$) and balloon predilation (97.4% vs. 79.3%, $P < 0.001$) [Supplementary Table 2, http://links.lww.com/CM9/A847]. Hemodynamics significantly improved after TAVR in both valve-type patients [Supplementary Table 3, http://links.lww.com/CM9/A847]. The in-hospital complication rates were not significantly different between the two groups [Supplementary Table 4, http://links.lww.com/CM9/A847]. However, patients with BAV had a lower incidence of in-hospital mortality (1.4% vs. 3.3%, $P = 0.043$) and 1-year mortality (2.3% vs. 5.8%, log rank $P = 0.083$) [Figure 2].

Discussion

Utilizing data from a multi-center registry from China, this study analyzed the characteristics and outcomes of TAVR candidates in China with respect to regions and valve morphology. The findings can be summarized as follows: (1) the Chinese TAVR candidates were relatively young, with a mean age of 73.8 ± 6.5 years; (2) the proportion of

Table 4: In-hospital clinical outcomes for patients undergoing TAVR (by regions).

Outcomes	Total	Northeast	Northwest	Southwest	Central-south	Central-east	Statistical values (Chi-square value)	P value
Number of patients, n (%)	1204 (100.0)	120 (10.0)	19 (1.6)	889 (73.8)	82 (6.8)	94 (7.8)		
All-cause mortality	2.2 (26/1204)	0.8 (1/120)	0 (0/19)	1.8 (16/889)	6.1 (5/82)	4.3 (4/94)	9.909	0.042
Cardiac mortality	0.9 (11/1204)	0.8 (1/120)	0 (0/19)	0.9 (8/889)	1.2 (1/82)	1.1 (1/94)	0.293	0.990
Stroke	0.7 (9/1204)	0 (0/120)	0 (0/19)	0.7 (6/889)	0 (0/82)	3.2 (3/94)	9.303	0.054
PPMI	11.0 (133/1204)	12.5 (15/120)	10.5 (2/19)	11.2 (100/889)	14.6 (12/82)	4.3 (4/94)	5.783	0.216
Atrial fibrillation newly-onset	0.6 (7/1204)	3.3 (4/120)	0 (0/19)	0.3 (3/889)	0.0 (2/82)	0 (0/94)	17.569	0.001
Coronary artery obstruction	0.6 (7/1204)	0.8 (1/120)	0 (0/19)	0.4 (4/889)	2.4 (2/820)	0 (0/94)	5.971	0.203
Myocardial infarction	0.2 (2/1204)	0.8 (1/120)	0 (0/19)	0.1 (1/889)	0 (0/82)	0 (0/94)	3.700	0.448
Cardiac tamponade	0.3 (4/1204)	0 (0/120)	0 (0/19)	0.4 (4/889)	0 (0/82)	0 (0/94)	1.422	0.840
Cardiac arrest	0.3 (4/1204)	1.7 (2/120)	0 (0/19)	0 (0/889)	0 (0/82)	2.1 (2/94)	20.007	<0.001
Major bleeding	0.5 (6/1204)	0 (0/120)	0 (0/19)	0.6 (5/889)	1.2 (1/82)	0 (0/94)	2.100	0.717
Major vascular complication	1.1 (13/1204)	0 (0/120)	0 (0/19)	0.9 (8/889)	6.1 (5/82)	0 (0/94)	25.062	<0.001

PPMI: Permanent pacemaker implantation; TAVR: Transcatheter aortic valve replacement.
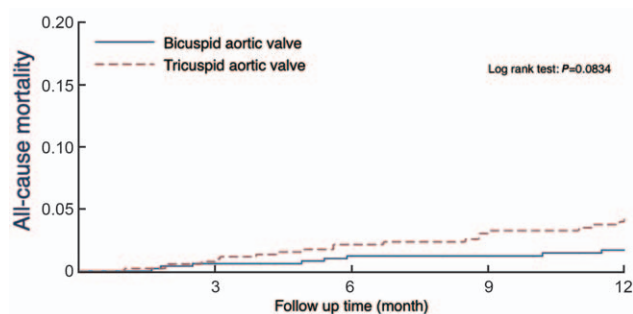
Figure 1: All-cause mortality after transcatheter aortic valve implantation at 1-year follow-up: by regions (n = 1204).
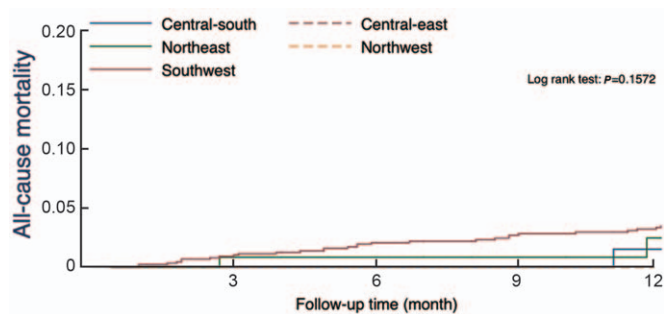
Figure 2: All-cause mortality after transcatheter aortic valve implantation at 1-year follow-up: by aortic valve morphologies (n = 1045).

BAV was relatively higher than that of TAV at 48.5%; (3) a vast majority of the TAVR procedure was performed using early generation valves; (4) hemodynamics were significantly improved after TAVR; (5) the 1-year mortality of TAVR recipients in China was 4.5%; and (6) the rates of post-procedural complications in patients with BAV were comparable to those with TAV, whereas the in-hospital and 1-year mortality rates were lower in the former. To the best of our knowledge, this is the first report of a multi-center registry in China.

As TAVR gains accelerating momentum across the globe, recognizing and acknowledging regional differences in patient characteristics and prognosis is crucial for the generalization of this rapidly growing technology.[1,12] Chinese patients who underwent TAVR present with distinct anatomical features that pose a challenge to the western standard.[8,13] The clinical profile and TAVR outcomes in China have been reported by some single-center studies, but there remains a paucity of population data at the national level.

The patient populations from previous western TAVR registries usually have a mean age of over 80 years. This is in accordance with data from the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapies (TVT) database (median age, 84 years) and the German Aortic Valve Registry (GARY) study (mean age, 81 years).[14,15] The low-risk Nordic Aortic Valve Intervention trial also had a mean age of 79.[16] The

major findings from CARRY agree with those from the previous studies conducted in Chinese patients and show that there is a higher proportion of BAV in the younger population. This is consistent with the data from the studies of surgical aortic valve replacement (SAVR), which demonstrated that the proportion of BAV was higher in young patients with AS and exceeds 60% in patients younger than 70 years.[17] In this study, BAV constituted 48.5% of the population. Concerned with the extreme elliptical morphology and severe calcification that negatively impact valve deployment, previous guidelines and expert consensus have established BAV as a relative contraindication.[18] However, with accumulating experience and progress in valve anchoring, researchers have begun to include patients with BAV in registries or trials.[19,20] Therefore, the high proportion of BAV in the current study enriches the TAVR experience in the BAV population and supports the rationale of expanding TAVR to low-risk patients.

Transfemoral access is associated with lower rates of procedure-related complications and long-term mortality. The superiority of transfemoral access over other vascular routes was further confirmed using Placement of Aortic Transcatheter Valves II data.[21] The majority of TAVR procedures are performed through a transfemoral access (98.2%) in China, which is higher than that in other registries or national databases.[14,22] This could be because TAVR took off late in China; consequently, operators favor a more established and safer route of

transfemoral access. This trend is mirrored in the Society of Thoracic Surgeons (STS)/TVT database, which showed that before 2013, transfemoral access was adopted in only 57.08%, and by 2019, the figure reached 95.26% ($P_{trends} < 0.001$).[14] The valve design itself is also an important feature in the early phase of TAVR implementation in China. Currently, four domestic TAVR devices and Sapien valves are commercially available in China. In CARRY, most of the TAVR was performed using domestic valves, in which Venus-A was the earliest to enter the market and is the most widely used. The domestic TAVR device has comparable safety and efficacy to the mainstay valves and can significantly improve hemodynamics. The rates of complications, including bleeding, vascular complications, and stroke, were lower than those in the previous studies, which may be explained by the more frequent use of transfemoral access.[10,23] Also, the mean age of the present population is relatively younger than that of previous studies, with lighter comorbidity burden. In the STS/TVT registry, incidences of coronary artery disease, atrial fibrillation, and prior cardiac surgery (62.8%, 41.9%, and 34%, respectively) were all higher than those in the present study. As TAVR took off late in China, the implementation of TAVR learned a lot from the experience obtained in other countries. In pre-TAVR work-up, all centers routinely used the contrast-enhanced CT where possible to comprehensively evaluate the anatomy and perform valve sizing. These factors jointly translated into a benefit in reducing post-procedural complications. Of note, the PPMI rate in this study (11.0%) was lower than that from other studies using early self-expandable valves (19.8% in the Corevalve high-risk study),[24] and is still lower than that in studies using late self-expandable valves (14.6% in the Evolut PRO subset from the STS/TVT database).[25] These findings are similar to the findings from previous studies.[19] One possible explanation is that the tapered inflow end and radiopaque makers from domestic valves may reduce the incidence of conduction disturbances. In addition, the 1-year mortality in our study was 4.5%, which is similar to the previous findings based on Chinese patients, but lower than that in other studies outside of China.[26] This may be associated with valve type, vascular access, and the younger population in China.

With accumulating experience and device iteration, BAV is no longer listed as an absolute contraindication for the TAVR procedure, but is still an indicator favoring SAVR, as stated by the current guidelines.[1] Early experience with first-generation valves showed that BAV was associated with higher rates of paravalvular leak, annular injury, and PPMI.[13] However, data from new-generation valves have shown similar safety and efficacy between BAV and TAV populations, and some studies have even reported lower mortality in patients with BAV.[27] This could be due to the evolution of the device and advancement along the learning curve. The effect of relatively younger age and lower burden of comorbidity in the BAV population on prognosis is no longer counteracted by the aforementioned complication. In this study, the mean age was comparable between the BAV and TAV patients, but the former was less frequently associated with hypertension, atrial fibrillation, and other comorbidities. Additionally, in response to the higher proportion of BAV in the Chinese TAVR population, domestic valves, such as Venus-A catered to the valve design to provide a stronger radial force, which allows for sufficient stent expansion under heavy calcification and raphe leaflets.[28] These encouraging findings from CARRY add to the evidence base that supports the expansion of TAVR in low-risk and BAV patients. Techniques such as cusp-overlap may also help streamline TAVR procedure.[29] Furthermore, as the current study did not use a core lab to unanimously assess valve morphologies, we failed to obtain the proportions of BAV subtypes and their prognostication. This is the inherent flaw of an observational registry, which was also seen in GARY and STS/TVT registries. In future studies, an attempt to collect images of key planes of the annulus to determine the morphology consistently is desired to address this issue.

Limitation

This study has several limitations that require further interpretation. Although CARRY covers several distinct regions across China, the initial phase only included seven centers, with considerable inter-center variability in terms of enrollment volume, resulting in less robust regional comparisons. However, the later phases of CARRY will provide further details in response to this limitation by continuously enrolling patients. Besides, the volume of different valves used varied significantly in the current cohort, with limited application of balloon-expandable valves. Therefore, we did not attempt to compare outcomes grouped by the type of available devices in this report. In addition, baseline data were absent in some patients due to the retrospective nature of this study, but this would be resolved in the prospective part of CARRY. Lastly, the mean follow-up duration was relatively short, with a low rate of long-term follow-up. Further results from CARRY will allow for the analysis of long-term clinical outcomes following TAVR in China.

Conclusions

CARRY is the first ever reported multi-center TAVR registry in China, which included 1204 patients from seven centers. The study found that TAVR candidates in China were younger, had a higher proportion of BAV, and had lower rates of post-procedural complications and mortality than other international all-comer registries. Given the use of early generation valves in the majority of the population, patients with BAV had similar rates of complications, but lower mortality compared to their TAV counterparts. These findings further propel the extension of TAVR in low-risk patients. Further inclusion of patients and long-term follow-up will more comprehensively delineate the patient profile and clinical outcomes in the Chinese TAVR population.

Conflicts of interest

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