Comparison of Procedural and 1-Year Clinical Results of Transcatheter Aortic Valve Implantation Using Prostheses with Different Design of Support Frame

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Summary

Our study aimed to investigate whether the frame design of transcatheter heart valve (THV) affects the procedural and clinical results of transcatheter aortic valve implantation (TAVI).

We retrospectively reviewed 163 patients with aortic stenosis who underwent TAVI using different types of THV (Edwards SAPIEN, n = 31; Venus-A, n = 63; and J-Valve, n = 69). The procedural outcomes and follow-up results for 1-year were compared among groups.

The patients who underwent TAVI using J-Valve had a higher mean transaortic pressure gradient than those using SAPIEN or Venus-A after TAVI (1-year follow-up; \(P = 0.017\), \(P < 0.001\), respectively), whereas no difference was observed between the patients with SAPIEN and Venus-A prosthesis (\(P = 0.150\)). The incidence of permanent pacemaker implantation was highest in patients with Venus-A (19.0%), followed by SAPIEN (9.7%), and lowest in J-Valve (4.3%) (\(P = 0.025\)). No difference was observed in the 30-day mortality rate among the groups (\(P = 1.000\)). Moreover, Kaplan-Meier survival analysis revealed that there was no significant difference in the 1-year cumulative patient survival rate among three patient cohorts (log-rank, \(P = 0.850\)).

The frame design of THVs could affect the valve-related hemodynamics and the incidence of permanent pacemaker implantation in TAVI, whereas it did not influence the survival rate of TAVI patients during 1-year follow-up period. All three THVs provided a convincing short-term outcome for TAVI patients.

(Key words: Transcatheter heart valve, Transaortic pressure gradient, Permanent pacemaker implantation)

Transcatheter aortic valve implantation (TAVI) has emerged as an alternative treatment for patients with aortic stenosis (AS) who are at intermediate to high risk for surgery,1,2 and the procedure exhibited a convincing long-term efficacy. With the emergence of new TAVI systems, transcatheter heart valve (THV) devices with different support frame designs were used in interventional treatment for aortic disease.3-6 THVs have their characteristic design of support frame structure such as J-Valve7 prosthesis that consists of a trifoliate porcine aortic valve mounted in a short self-expandable cylinder nitinol stent. Edwards SAPIEN8 prosthetic valve has a similar configuration in the support frame with J-Valve, but it was made of cobalt-chromium alloy and released by balloon dilation. Besides, a long self-expandable nitinol frame was adopted by Medtronic CoreValve9 or Venus-A10 or VitaFl ow11 and others.

The feasibility and convincing short-term outcome of J-Valve was reported in our previous study.4,12 However, compared with the reported results of other THVs,13,14 it was observed that the patients treated with J-Valve showed a relatively higher transaortic pressure gradient. We speculated the phenomenon attributing to the frame design of this prosthesis. To date, no evidence showed that the frame design of THV could affect valve-related hemodynamics after TAVI, and it has not been well investigated whether procedural and clinical outcomes could be influenced by the frame design of prosthesis.

In this study, we compared the procedural, valve-related hemodynamic and short-term follow-up results between patients who underwent TAVI using THVs with different frame designs (Edwards SAPIEN or Venus-A or J-Valve), which aimed to evaluate the effect of prosthetic frame design on TAVI results.

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Methods

Patient selection: The local ethical committee approved this study protocol, and signed informed consents were obtained from all enrolled patients. The study population included patients with severe AS who underwent TAVI in three cardiac centers in China. The key clinical inclusion criteria were as follows: (1) severe symptomatic AS with aortic valve area < 1.0 cm² or mean transvalvular pressure gradient > 40 mm Hg or peak velocity > 4 m/second, (2) New York Heart Association (NYHA) functional class II or higher, and (3) STS score of 4% or greater. The exclusion criteria were as follows: acute myocardial infarction (≤ 6 weeks prior to the procedure), left ventricular ejection fraction (LVEF) < 20%, severe coronary artery disease, end-stage renal disease, and cerebrovascular events within the previous 6 months. Anatomical exclusion criteria included aortic annulus diameter < 19 mm or > 27 mm, mitral or tricuspid valve regurgitation (≥ moderate degree), and an ascending aortic diameter > 45 mm.

A total of 69 patients with severe symptomatic AS who were treated with J-Valve (JieCheng Medical Technologies, Suzhou, China) were included between March 2014 and July 2017. Of these patients, 64 participated in J-Valve China clinical trial at three cardiac centers (Fuwai Hospital, West China Hospital, and Zhongshan Hospital) to get official approval from China Food and Drug Administration. From December 2012 to April 2016, 63 patients treated with Venus-A THV (Venus MedTech, Hangzhou, China) were also enrolled in this study. Among them, 48 patients participated in the clinical trial of Venus-A at our institution to obtain a license from China Food and Drug Administration for clinical use. In addition, we enrolled 31 patients with AS who participated in Edwards SAPIEN (SAPIEN-XT or SAPIEN-3) (Edwards Lifesciences, Irvine, CA, USA) China clinical trial at our institution.

TAVI Devices and Procedures: The J-Valve aortic valve prosthesis consists of a set of porcine aortic valve mounted and sutured in a short cylindrical self-expanding nitinol stent. The ingenious design of J-Valve is a positioning element made up of three U-shaped nitinol graspsers that could orient and position to the Valsalva sinus. Venus-A THV is made of a long self-expandable nitinol frame that has a flared upper portion and consists of a tri-leaflet porcine pericardial valve. SAPIEN-XT and SAPIEN-3 are balloon-expanding THVs, which consist of three bovine pericardial tissue leaflets mounted and sutured in a short cylinder cobalt-chromium frame. All patients received TAVI under fluoroscopic guidance and local and/or general anesthesia. The procedures of THV implantation have been described in detail in previous studies. All patients who underwent TAVI received warfarin anticoagulant therapy for half a year.

Echocardiography and follow-up: Transthoracic echocardiography was used to evaluate valve hemodynamics and cardiac function. The sonographic data were collected and analyzed including the terms of peak systolic velocity, transaortic pressure gradient, paravalvular leakage, LVEF, left ventricular end-diastolic diameter, morphological structure, and others. Periodical outpatient visits and telephone interviews were performed to obtain clinical status and echocardiographic follow-up data at discharge, 1 month, 6 months, and 1 year.

Statistical analysis: The distribution normality of continuous data was assessed using the Shapiro-Wilk test. Continuous variables were expressed as mean ± standard deviation or median (interquartile range), as appropriate. Categorical variables were presented as number (n) and percentage (%). Comparisons of continuous variables among the three groups were performed using Kruskal-Wallis test or one-way analysis of variance (ANOVA) with Bonferroni or Tamhane post hoc test. For time-dependent variables, repeated measures ANOVA with Bonferroni post hoc test were performed. Comparisons of categorical variables among the groups were tested using Pearson chi-square test or Fisher’s exact chi-square test. In addition, 1-year survival probability was estimated from the Kaplan-chi-square test or Fisher’s exact chi-square test. In the incidence of PPI between different THVs, the incidence of PPI was highest in patients with Venus-A (19.0%), followed by Edwards SAPIEN (9.7%), and lowest in J-Valve (4.3%). Considering the pairwise comparison, the incidence of PPI for patients treated with Venus-A was significantly higher than that for patients with J-Valve (P = 0.012). Although the incidence of PPI was slightly higher in the patient’s cohort with Venus-A than with SAPIEN;
However, the difference was not statistically significant ($P = 0.370$). Similarly, there was no difference between SAPIEN and J-Valve cohort ($P = 0.371$). The procedural characteristics were presented in detail in Table III.

**Hemodynamic performance:** During the follow-up period, no morphological structural valve deterioration was observed in all enrolled patients. There were no patients who underwent redo TAVI and no death associated with THV deterioration. The mean transaortic pressure gradient decreased from $57.05 \pm 15.86$ mm Hg (pre-TAVI) to $13.89 \pm 7.39$ mmHg (discharge) in these patients ($P < 0.001$). There was no difference in the mean transaortic pressure gradients among the three cohorts before TAVI procedure ($P = 0.348$), whereas the higher mean pressure gradient was observed in patients who used J-Valve than SAPIEN and Venus-A at the reported time points post-implantation (Figure 2). No difference was observed in mean transaortic pressure gradients between Edwards SAPIEN and Venus-A cohort after TAVI (Figure 2). In patients with SAPIEN or J-Valve prostheses, no difference was observed in mean transaortic pressure gradient among the reported time points following TAVI procedure ($P = 0.143$, $P = 0.424$, respectively). Moreover, there was no difference in transaortic pressure gradient at each time point after discharge in patients with Venus-A ($P = 0.234$). We also compared the incidence of mild or more than mild paravalvular regurgitation among the three patient cohorts, and no statistical difference was observed between them at the reported time points after TAVI procedure (Figure 3). Other echocardiographic findings are presented in Table II.

**Clinical outcomes:** The mean LVEF of the three patient cohorts gradually increased with time during the follow-up period. Compared with pre-operation, the mean LVEF significantly increased in Venus-A and J-Valve cohort at 1-year follow-up ($P < 0.001$ and $P = 0.002$; Table II). Although the statistical difference did not reach, the increased mean LVEF at 1-year follow-up was also observed in SAPIEN cohort (Table II). Most of the patients (90.8%) were in NYHA functional class II at 1-year follow-up, indicating that the majority of patients could potentially benefit from TAVI procedure to improve car-
The 30-day mortality rates were 6.5%, 4.8%, and 5.8% in Edwards SAPIEN, Venus-A, and J-Valve cohorts, respectively \((P = 1.000)\). All-cause morbidity rate was 7.4% in all enrolled patients at 1-year follow-up. Kaplan-Meier survival analysis revealed that there was no significant difference in the 1-year cumulative patient survival rate among three patient cohorts \((\text{SAPIEN, } 93.5\%; \text{ Venus-A, } 93.7\%; \text{ J-Valve, } 90.8\%; \text{ log-rank, } P = 0.850; \text{ Figure 4})\).

### Discussion

Our results demonstrated that the patients who underwent TAVI using J-Valve have a higher transaortic pressure gradient than those using Edwards SAPIEN and Venus-A. However, the incidence rate of PPI was highest in patients with Venus-A, followed by Edwards SAPIEN, and lowest in J-Valve. Morphological structural degeneration of prosthesis was not observed in all enrolled patients during follow-up. Furthermore, there is no difference in survival rate at 30 days and 1-year follow-up. All three types of THV presented a convincing short-term clinical outcome. Our results indicated that every THV has its advantages in TAVI treatment.

In our previous study, the possible reasons why J-Valve had a higher transaortic pressure gradient after TAVI were analyzed. We speculated that its frame design may be a possible reason because THV is not fully expanded after implantation (Figure 5), which implies that its support frame cannot exert enough radial force on the calcified aortic valve. The J-Valve prosthesis is a second-generation THV, which consists of a trifoliate porcine aortic valve mounted in a short self-expandable cylinder nitinol alloy stent. The positioning element is the ingenious design made up of three U-shaped nitinol graspers that joined together by three sliding tracks, which could orient and position to the Valsalva sinuses. It is connected with the support frame by connecting sutures attached with three sliding tracks. Placement of the positioning casper in Valsalva sinuses could facilitate the accurate deployment of THV during TAVI procedure. Besides, the native valve leaflets are clamped between the support frame and positioning element, which facilitates the strong anchoring of THV at the aortic position. Hence, although the short self-expandable cylinder stent could not exert enough radial forces to support the calcified aortic valve, J-Valve prosthesis can also be stably anchored at the location of native aortic valve. Due to the flexible connection with sutures between the positioning element and valve body, the rough positioning of nitinol graspers did not affect the deployment of valve body. J-Valve can also be used for patients with Sievers’ Type-1 bicuspid aortic valve whose valves are potentially tricuspid. The structural design of J-Valve is more beneficial to the transcatheter interventional treatment in patients with pure aortic regurgitation. However, the radial force of its support frame

### Table III. Procedural Characteristics

| Access             | SAPIEN \((n = 31)\) | Venus-A \((n = 63)\) | J-Valve \((n = 69)\) | \(P\) value |
|--------------------|---------------------|----------------------|----------------------|-------------|
| Transfemoral       | 31 (100.0)          | 55 (87.3)            | N/A                  |             |
| Access             | N/A                 | N/A                  | 69 (100.0)           |             |
| Transapical        | N/A                 | N/A                  | 8 (12.7)             |             |
| Transaortic        | Type of anesthesia used |                      |                      | N/A         |
| General/conversion to general | 6 (19.4)    | 24 (38.1)            | 69 (100.0)           |             |
| Procedural success | 29 (93.5)           | 60 (95.2)            | 64 (92.8)            | 0.913       |
| Pre-dilation       | 29 (93.5)           | 63 (100.0)           | 69 (100.0)           |             |
| Post-dilation      | 7 (22.6)            | 9 (14.3)             | 18 (26.1)            |             |
| Operation time, minutes | 118.00  | 97.50 (85.50–127.50) | 105.00 (89.00–122.75) | 0.083       |
| Conversion to open heart surgery | 1 (3.2)    | 3 (4.8)              | 5 (7.2)              | 0.740       |
| Causes for conversion |                      |                      |                      | N/A         |
| LV perforation     | 1 (1.6)             |                      |                      |             |
| THV mispositioning | 1 (3.2)             | 4 (5.8)              |                      |             |
| Coronary artery obstruction | 1 (1.6)    |                      |                      |             |
| Aortic annular rupture | 1 (1.6)        |                      |                      |             |
| Severe paravalvular leak | 1 (1.4)    |                      |                      |             |
| CPB using          | 1 (3.2)             | 2 (3.2)              | 4 (5.8)              |             |

Continuous variables are expressed as median (interquartile range). Categorical variables are presented as \(n (%)\). N/A indicates not applicable; LV, left ventricular; THV, transcatheter heart valve; and CPB, cardiopulmonary bypass.
may not be enough for patients with severe calcification of aortic valve.

These did not mean that J-Valve is not a well-designed THV for patients with AS. We observed that the rate of PPI was significantly lower in patients who were treated with J-Valve (4.3%) than in those who were reported with Edwards SAPIEN\textsuperscript{22,23} or Medtronic Core-Valve\textsuperscript{24} or other THVs\textsuperscript{11,25,26}. We speculated the reasons for the lower rate of PPI in patients using J-Valve as follows: (1) The connecting sutures between valve body and positioning element\textsuperscript{7} can prevent deep positioning of the prosthesis within left ventricular outflow tract during THV...
Figure 4. Kaplan–Meier survival curves of three prosthesis cohorts from all-cause death at 1-year follow-up

|                | Pre-operation | Discharge | 1-Month | 6-Months | 1-Year |
|----------------|---------------|-----------|---------|----------|--------|
| SAPIEN         | 31            | 28        | 28      | 28       | 28     |
| Venus-A        | 63            | 60        | 60      | 60       | 59     |
| J-Valve        | 69            | 62        | 60      | 58       | 57     |

Figure 5. Lateral chest radiograph at 1 month after J-Valve implantation. Black arrow indicates the inadequate expansion of support frame at the upper portion

deployment. In TAVI procedure, this is an effective way to avoid the complete AV block that may directly result from the compression caused by THV devices, leading to a lower incidence of third-degree AV block. (2) The lesser radial force of support frame could reduce excessive compression on calcified aortic valve/annular, which may be
another contributing factor to this advantage of J-Valve.

Venus-A is the first THV that has been certified for clinical use in China, which is designed with a long self-expandable nitinol stent. In our cohort, 19.0% of the patients who received Venus-A prosthesis required a new PPI in accordance with the patients with an implanted CoreValve or VitaFlow 

The frame design of THVs affected procedural and hemodynamic results of TAVI. The published findings of this study were still in its early stage in China. A study with a larger sample size and longer follow-up durations is subsequently needed to confirm the findings of this study. Since a large time span among the three clinical trials and the randomicity of patient selection, there are differences in some baseline characteristics among the three patient cohorts. Besides, the procedural characteristics are quite different. Implantation of J-Valve needs transapical approach and general anesthesia, whereas the other two THVs do not. Furthermore, there are many THVs currently being used on a global scale, but we have only selected three types of THV used in China. The effect of other frame designs of THV on TAVI outcomes still needs to be carried out in subsequent studies.

Conclusion

The frame design of THVs affected procedural and hemodynamic results of TAVI. However, no difference in 30-day morbidity rate and 1-year cumulative survival rate were observed among the three types of prosthesis, indicating that all three THVs provided a convincing short-term outcome. Our findings could provide evidence for the improvement strategies of the THV frame design to achieve better hemodynamics and reduce the incidence of PPI in TAVI patients.

Disclosure

Conflicts of interest: The authors declare that they have no conflict of interest.

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