CLINICAL STUDY

Long-Term Outcomes of Patients with Self-Expandable Transcatheter Heart Valve Embolized in the Aorta

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Summary

This study assesses the long-term outcomes of patients who suffered from self-expandable transcatheter heart valve (THV) embolized in the aorta in transcatheter aortic valve implantation (TAVI).

We retrospectively reviewed the patients with self-expandable THV embolized in the aorta. Follow-up computed tomography was performed to assess the THV migration, strut fractures, and device-related aortic complications.

Of the 539 TAVI patients, 11 suffered from self-expandable THV embolized in the aorta. Two patients underwent open-heart surgery to remove the embolized THVs in the ascending aorta. Embolized THVs were repositioned in the aortic arch distal to the left subclavian artery (n = 3) and the thoracic descending aorta (n = 6). Three patients died during a median follow-up time of 40 months. The remaining eight survivors presented with New York Heart Association functional class I or II at the last follow-up. Degeneration of embolized prostheses with thick leaflets and rolled cusp edges was observed in three patients. There was no evidence of valve migration, strut fracture, prosthesis-associated aortic complication, and thrombosis attached on embolized valve for all patients with THVs repositioned in the aorta.

Self-expandable THV embolization can be effectively managed in TAVI. Although some embolized valves exhibited leaflet degeneration, the long-term safety of repositioning embolized self-expandable THV in the aorta is assured.

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Key words: Transcatheter aortic valve implantation, Self-expandable prosthesis, Embolization, Thoracic descending aorta, Aortic arch

Transcatheter heart valve (THV) embolization is a rare but an ineluctable complication surrounding transcatheter aortic valve implantation (TAVI)15 regardless of the type of prosthesis used. As a conservative bail-out maneuver, embolized THVs in the ascending aorta could be managed by withdrawing and repositioning them in a secure region of more distal aorta without obstructing important aortic branches.2-5) The clinical outcomes and hemodynamic consequences of embolized valves remain good over mid-term follow-up period in patients who had embolized Edwards SAPIEN THV (a balloon-expandable prosthesis) in the aortic arch or thoracic descending aorta.6) However, this revealed evidence may not be fully applicable to self-expandable valves as the stent deployment method of self-expandable valves is completely different from that of balloon-expandable valves. The support frame of embolized self-expandable THV is made of nickel-titanium alloy with temperature-dependent shape memory properties.6-9) They may exert additionally continuous pressure on the aortic wall after the prostheses are placed in an ectopic site.

During TAVI, THV embolization can occur when a self-expandable prosthesis is partially or completely deployed. Partially deployed first-generation THVs should be withdrawn and placed in a more distal position (thoracic descending aorta or abdominal aorta).10) Encouragingly, the second-generation THV system can retrieve the prosthesis to reposition it in the correct annular position before the final deployment,11) which significantly decreases the incidence of valve embolization. However, THV embolization was still deemed as an unavoidable complication after the final deployment of the first- or second-generation prosthesis. These embolized valves were commonly retracted and repositioned in the ascend-
ing aorta or aortic arch, which has been widely reported in many THVs, such as Medtronic CoreValve, Portico, Lotus, and Accurate NEO.

To date, there is a significant number of patients who had embolized THV in the aorta due to the fact that over 100,000 THV implantations were currently performed for aortic disease each year, accounting for a high proportion of first-generation devices that are more prone to developing embolization surrounding TAVI, but limited evidence is available for the long-term outcomes of these patients. In this study, we reviewed and followed up the patients who suffered from self-expandable THVs embolized in the aorta, with the aim of providing more evidence for the long-term clinical outcomes and the long-term safety of embolized self-expandable prostheses placed in an ectopic site.

Methods

Study population: Our study was approved by the ethics committee of Fuwai Hospital. We retrospectively reviewed all patients undergoing TAVI for severe aortic stenosis or bioprosthetic valve failure between January 2012 and July 2020 in our institution, with the aim of identifying the cases who suffered from THV embolized in the ascending aorta. Of the 539 TAVI patients in our institution, 11 were identified as eligible for this study.

TAVI devices and procedures: J-Valve prosthesis (Jiecheng Medical Technologies, Suzhou, China), Venus-A prosthesis (Venus MedTech Technologies, Hangzhou, China), and VitaFlow prosthesis (MicroPort, Shanghai, China) were used in 2, 8, and 1 patient, respectively. J-Valve is a second-generation THV implanted transapically, which is a short, cylindrical, self-expandable nitinol support frame that has been mounted and sutured with a trifoliate porcine aortic valve. A positioning element of three U-shaped nitinol graspers joined together by three sliding tracks is movably attachable to the valve body by three connecting sutures, facilitating the positioning of the prosthesis in the native aortic annular not only for aortic stenosis but also for pure aortic regurgitation. Venus-A valve is a first-generation THV and features a long, self-expandable nitinol stent with sutured bioprosthetic valve leaflets made from porcine pericardium. The VitaFlow prosthesis consists of a trileaflet bovine pericardial valve that is mounted on a self-expanding nitinol stent frame. Initial TAVI procedures were performed via transfemoral or transapical approach under local or general anesthesia with fluoroscopic guidance and transesophageal echocardiogram monitoring. Previous studies described these THV systems and the TAVI procedures in detail.

Follow-up: Clinical, procedural, and echocardiographic characteristics during hospitalization were obtained from an electronic medical record system. Follow-up information was obtained through outpatient clinic visits or by contacting the patient or their families through telephone. Embolized THVs were assessed via computed tomography (CT) examination to evaluate the occurrence of aortic complications and to identify the leaflet degeneration, position, and structural integrity of the embolized THV.

Statistical analysis: The Shapiro-Wilk test was conducted to determine whether the continuous variables fit a normal distribution. Normally distributed variables were expressed as mean values with standard deviations, whereas non-normally distributed variables were expressed as median with interquartile interval. Categorical variables were expressed as number. Paired t-test was employed where appropriate. Statistical analysis was conducted using the SPSS software version 25.0 (IBM Corp., Armonk, NY, USA).

Results

Baseline characteristics: The mean age of the patients was 76.09 ± 6.75 years. Three were identified as New York Heart Association (NYHA) functional class II patients and eight as class III patients. Of them, eight had hypertension, three had atrial fibrillation, two had type II diabetes, and six had coronary artery disease. The mean score of Society of Thoracic Surgeons Predicted Risk of Mortality was 7.00% ± 1.76%.

Prior to the TAVI procedure, the mean transaortic pressure gradient was 50.91 ± 25.26 mmHg; mean aortic valve orifice area, 0.77 ± 0.42 cm²; left ventricular ejection fraction, 61.73% ± 8.24%; and left ventricular end-diastolic diameter, 52.73 ± 10.35 mm. Native aortic valve was tricuspid in eight patients, pseudo-bicuspid (Sievers’ type I) in two patients, and true-bicuspid (Sievers’ type 0) in one patient. The baseline characteristics are presented in detail in Table I.

Procedural settings and cause of embolization: In the initial TAVI procedure, J-Valve, Venus-A, and VitaFlow prostheses were used for two, eight, and one patient, respectively. General anesthesia was induced in four patients, and three patients were shifted from local anesthesia to general anesthesia after THV embolization because open-heart surgery was needed for an emergency situation. The other four patients were operated on under local anesthesia throughout the TAVI procedure. More details are presented in Table II.

Of the eight patients with Venus-A prosthesis, six suffered from dislodging of partially deployed valves from the native annular position. The most common reason was the deployment of prosthesis at a high level, followed by inadequate visualization of the valve plane and premature termination of pacing. These embolized valves were retracted and placed in the thoracic descending aorta, in a stable region with no obstruction of important aortic side branches (Figure 1A-D). A second THV was implanted in the correct annular position in five of the patients (Figure 1E-H), and another patient underwent annular repair and conventional aortic valve replacement after explorative thoracotomy due to pericardial tamponade caused by aortic annular rupture. There was one patient who suffered from THV embolization after the final deployment. For this patient, the TAVI procedure was switched to open-heart surgery without delay to remove the embolized prosthesis from ascending aorta and replace the native aortic valve with Carpentier-Edwards Perimount bioprosthesis. Moreover, one patient suffered from embolization of a completely deployed Venus-A valve in the ascending aorta as well as from aortic wall injury, which resulted in Stan-
stroke associated with the initial TA VI procedure and bail-out maneuver did not occur in all of the patients.

In one patient in which J-Valve was used, the U-shaped claspers failed to position the aortic sinus, which resulted in the valve body not being deployed in the correct position of aortic annulus; the prosthesis was consequently dislodged into the ascending aorta (Figure 2A, B). The embolized J-Valve prosthesis was retracted using snare catheter to reposition it in the aortic arch distal to the left subclavian artery. This prosthesis flipped vertically out of position in this patient (Figure 2C, D). The embolized J-Valve prosthesis occurred in another patient after the apical guidewire was pulled out. In this patient, the bulky deposit deriving from diffuse nodular cal-
cification of aortic valve and aortic annulus bulged into Valsalva sinuses. As a result, the U-shaped graspers of positioning key were partially stuck in the aortic sinuses.

The partially positioned U-shaped claspers failed to settle at the bottom of the aortic sinuses, leading to the misplacement of the positioning key. Thereby, the valve body

**Figure 1.** Patient #8 during the Venus-A prosthesis implantation. A–C: Embolization of partially deployed Venus-A valve in the ascending aorta; D: embolized prosthesis displaced in the thoracic descending aorta; E–H: successful deployment of a second Venus-A prosthesis.

**Figure 2.** Patient #1 during the perioperative period of J-Valve implantation. A, B: Embolization of the J-Valve prosthesis in the ascending aorta; C, D: successful deployment of a second J-Valve prosthesis. E: ascending aorta aortogram showing adequate aortic perfusion distal to vertically flipped J-Valve prosthesis; F: chest X-ray radiography (6 hours after TAVI) showing embolized J-Valve prosthesis translocated to the thoracic descending aorta. The embolized J-Valve prosthesis is marked with black arrow.
was deployed too high within the annulus because the suture connection between the positioning key and the struts can prevent the support frame from lowering. After valve embolization, the dislocated prosthesis was pushed by blood flow into the ascending aorta with a vertical flip and then stuck at the position of the aortic arch distal to the left subclavian artery without percutaneous management. TAVI was switched to urgent open-heart surgery for this patient due to hemodynamic compromise. Although prosthesis flip occurred in the two aforementioned patients, surgical removal of embolized THVs was not necessary as the blood flow distal to the embolized prosthesis was evident in the ascending aorta aortogram (Figure 2E).

Follow-up: Patients were followed up at a range of 18 to 75 months with a median follow-up of 40 months. Of them, eight patients were still alive and in NYHA functional class I or II. One patient (Case #5) suddenly died on the way home on the day of hospital discharge. The patient experienced syncope while walking and lost consciousness, and the following rescue treatment was ineffective. There was also one patient (Case #3) who died of unexplained non-cardiac causes at 70 months after TAVI, and another patient (Case #10) died of multi-organ failure at 27 months after the emergency conversion from TAVI to surgery.

Transthoracic echocardiography was performed on ten patients (excluding Case #5) in follow-up period (median: 33 months), and it revealed a significant increase in aortic valve orifice area (1.51 ± 0.23 cm²; pre-operation versus the last follow-up, \(P = 0.001\)) with a concomitant reduction of aortic transvalvular pressure gradient (14.30 ± 7.04 mmHg; pre-operation versus the last follow-up, \(P = 0.002\)). Among patients with a second “in-series” prosthesis implantation at native annular position, five had mild paravalvular regurgitation at follow-up.

Follow-up CT images of eight patients who had embolized THV in the thoracic descending aorta or aortic arch distal to the left subclavian artery were obtained at a median of 33 months (range, 12-72 months) (Figure 3A-L). Three patients exhibited dysfunctional leaflets of embolized valve with thick leaflets and rolled cusp edges (Figure 3B-D, F-H). Compared with the final fluoroscopic
images, significant migration of the embolized prostheses was not observed in any of the patients. Moreover, CT imaging revealed no evidence of strut fracture, prosthesis-associated aortic complication, and thrombosis attached on the embolized valves.

Discussion

The patients who suffered from THV embolized in the aorta were followed up in this study. Of the 11 patients, 8 were still alive during the last follow-up. Leaflet degeneration of embolized valves was observed in three patients based on follow-up CT images. The cusp of these prostheses was thick with rolled free edge and held in closed position by commissural fusion. All of the embolized THV's were still in a stable position, with no evidence of device migration, strut fracture, THV-associated aortic complication, and thrombosis attached on the embolized valve. The placement of the embolized THV in the aorta is a bail-out maneuver with a reliable long-term safety.

Valve embolization inevitably occurs after THV implantation. However, the incidence of THV embolization has significantly decreased due to the development of techniques and the increase in operator experience.19) Correct patient selection could also effectively avoid embolization. Makkar, et al.19) reported that THV embolization is associated with anatomic factors, including lower mean aortic valve gradient, marked paucity of aortic valve calcification, and larger aortic annular. Given these risks, TAVI must be carefully considered in patients with the aforementioned anatomic features. If the interventional therapy is unalternative for them, manipulation of valve implantation should be cautiously performed by experienced operators. Moreover, other anatomic factors, such as kinking of thoracic or abdominal aorta and unfavorable angulation of the aortic root, which complicates catheter manipulation, could also increase the incidence of THV embolization in transfemoral TAVI.20) Transapical TAVI may be superior in these patients.

Venus-A prosthesis is a first-generation THV that cannot be recaptured and repositioned after the initiation of the valve deployment procedure. If partially deployed Venus-A valve is dislodged from the annular position, the partially detached prostheses will be withdrawn in the thoracic descending aorta or abdominal aorta and placed in a region without the obstruction of important side branches of aorta.10,12) The Venus-A Plus™ system is the new iteration of the Venus-A system to redesign the delivery system and modify the support frame of the prosthesis, which allows to recapture the partially deployed prosthesis after THV dislocation and then place it in the correct annular position. There are also other contemporary TAVI devices used in clinical practice worldwide, such as Medtronic Evolut R, Boston Lotus™, St. Jude Portico, and Direct Flow Medical®, each with unique characteristics.20,23) These new-generation THV's were designed to be fully retrievable to minimize the incidence of device embolization and have been the first choice in recent years.21)

Although the rate of valve embolization has significantly decreased with the advances in second-generation THVs and the improvement of their delivery system, this potentially life-threatening complication still can occur in the new-generation THVs after the final deployment of prosthesis. Giannini, et al.14) reported a case in which embolization of the Lotus valve occurred in the ascending aorta. The patient underwent bail-out maneuver to place the device in the thoracic descending aorta. Moreover, another case with Portico valve embolization was also reported by Giannini, et al.14) and the device was snared using Storq guidewire from the femoral artery and retracted to be placed in the ascending aorta. If THV embolization occurs after the final deployment, percutaneous maneuver with placement of the embolized THVs in a stable position in the aorta will be the first choice to manage this procedure-related emergency based on a short-term safety15,14,22) and the high 30-day mortality rate of urgent cardiac surgery.23,24)

J-Valve embolization can occur immediately after valve deployment. Holding the apical guidewire for a few minutes after the final deployment of the J-Valve prosthesis is a more robust strategy. When THV embolization occurs, the use of apical guidewire can prevent the inversion of the dislocated valve. It is favorable to change femoral arterial guidewire and advance a balloon within the embolized valve to reposition it at a stable position of more distal aorta. In published series,13,25) percutaneous management with snares was commonly employed to reposition self-expanding THVs, such as Medtronic CoreValve and Portico valve,25,26) in a stable region of the aorta when embolization occurred. However, it is not a suitable bail-out strategy for embolized J-Valve because the prosthesis could flip vertically during the pull-back maneuver with snare, increasing the risk of aortic injuries.

Patients with bicuspid aortic valve are likely to have an enlarged ascending aorta,26) and it is sometimes difficult to fix the embolized valve in the dilated aortic lumen. Moreover, it is difficult to manipulate the embolized valve with snares to place it in a stable position of distal aorta, because the valve may flip vertically or even invert in the wide intra-ascending aorta during the bail-out procedure. For these patients, percutaneous manipulation with balloon catheter may facilitate in retracting the embolized valves and then placing them in the site where the lumen of the aorta has a size that is equal to the THV outflow. If the embolized self-expandable THV repositions unstably in the new location, it could be further retracted and placed in a stable position of a more distal aorta using a snare catheter.

All patients in our study were administered vitamin K antagonist for 6 months after TAVI.17,27) Evidence of thrombus on the embolized valves was not found in the patients, as indicated by the follow-up CT images, and no thromboembolic event associated with embolized THVs occurred during the follow-up period. In Tay’s study,3) thrombus on the embolized prosthesis was observed in one patient, which then fully resolved after anticoagulant therapy. Although numerous cases of THV embolization in the aorta have been reported worldwide, the administration of prophylactic anticoagulants for antithrombotic treatment was not recommended for these patients. Anti-
coagulant therapy with vitamin K antagonist or a combination of low-dose aspirin and clopidogrel for 3-6 months after TAVI was recommended in the current practice guidelines. Due to the theoretically increased thromboembolic risk for patients with embolized THVs in the aorta, additional lifelong antiplatelet treatment with aspirin 75-100 mg daily after the recommended anticoagulation therapy may be a more appropriate therapeutic strategy. To date, limited evidence is available in this field; more results of long-term outcome should be obtained for these patients.

**Limitations:** This study has two major limitations: first is the limited number of patients recruited from our institution, and second, insufficient follow-up time for some patients who had embolized Venus-A prosthesis in the aorta. Therefore, longer follow-up duration and a larger sample size is required to warrant our results.

**Conclusions**

THV embolization can be effectively managed with good long-term clinical outcomes. The leaflets of embolized THVs that are repositioned in the aorta degenerate over time. There is no evidence of valve migration, strut fracture, aortic complications, and prosthesis-associated thromboembolic events. The long-term safety of repositioning embolized self-expanding valves in the aorta is assured.

**Disclosure**

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

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