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Predictors, Outcomes and Prevention of Stroke after Transcatheter Aortic Valve Replacement

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Abstract

Background— Every year more than 60,000 valve replacements are performed, and aortic valve replacement is the most common intracardiac procedure performed in the United States. Stroke is one of the most concerning complication of aortic valve replacement associated with increased mortality.

Methods— We performed a narrative literature review, enhanced by hand-search of the reference lists of included articles and relevant reviews.

Results— Intraprocedural embolic events are most common etiology for ischemic stroke associated with both surgical aortic valve replacement and transcatheter aortic valve replacement. Acute and subacute strokes after transcatheter aortic valve replacement have been reported in 3% to 9% of patients, with majority of them occurring within first month. Post-procedural stroke is associated with increased mortality after both surgical and transcatheter aortic valve replacement. Predictors of stroke include female gender, diabetes mellitus, calcification of ascending aorta, left ventricular ejection fraction <40%, acute kidney injury, peripheral vascular disease, previous stroke, walking < 300 meters during 6-minute walk test, concurrent carotid stenosis, and emergency department admission. Transfemoral transcatheter aortic valve replacement is the preferred approach and nonfemoral access is only used in 6% to 10% of patients in the United States. Transapical access seems to have rates of stroke comparable with transfemoral approach. On contrary, studies reporting subclavian/transaxillary access have yield contradictory results regarding stroke risk. The use of cerebral protection devices, such as Food and Drug Administration approved Sentinel device during transcatheter aortic valve replacement, may be associated with a lower rate of stroke at 30-days.

Conclusions— The rate and predictors of ischemic stroke associated with both surgical and transcatheter aortic valve replacement need to be recognized. The use of cerebral protection devices during transcatheter aortic valve replacement maybe associated with a lower 30-day stroke rate with transcatheter aortic valve replacement procedures.

Keywords— Transcatheter aortic valve replacement, surgical aortic valve replacement, stroke, cerebrovascular event, cerebral protection devices, mortality.

INTRODUCTION

Valvular heart disease (VHD) is a common condition in clinical practice that is associated with left ventricle (LV) dysfunction and death. The prevalence of valvular heart disease is 2.5% in developed countries, and expected to increase due to aging population (1). In developing countries, rheumatic heart disease remains the primary cause of valvular heart disease (2). Aortic valvular stenosis is the most prevalent primary valve disease in developed countries (3, 4). Since the prevalence of aortic stenosis is increasing with increasing age of population, management of aortic valvular stenosis is an important health issue (5).

Aortic valvular stenosis is a degenerative disease causing left ventricular outflow obstruction, decreased cardiac output, and subsequent death (6). Once patients become symptomatic, survival is approximately 50% in next two years (7). In the past, the only effective guideline-based treatment for aortic stenosis has been surgical aortic valve replacement (8, 9). The first prosthetic aortic valve replacement was performed in 1951 by Charles Hufnagel (10). After the heart-lung machine was developed, other advancements followed, such as the

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first aortic valve homograft which was performed by Donald Murray in 1956. In early 1960s, the first orthotopic prosthetic aortic and mitral valve replacement was performed (15). Patients who underwent surgical aortic valve replacement revealed an annual stroke rate of 1.3% vs 1.4% for bio prosthesis compared to mechanical valves (11). However, many patients with severe symptomatic aortic stenosis had multiple comorbid conditions and were considered high surgical risk for surgical aortic valve replacement, A less invasive treatment like transcatheter replacement was considered an alternative option (12). Since the first transcatheter aortic valve replacement was performed by Alan Cribier in 2002, it has been performed in approximately 300,000 patients in 65 countries (13, 14). The number of procedures has increased exponentially, and transcatheter aortic valve replacement is expanding as an option for younger and average surgical risk patients (15, 16).There are approximately 189,836 (95% confidence interval: 80,281 to 347,372) existing transcatheter aortic valve replacement candidates in the European countries and 102,558 (95% confidence interval: 43,612 to 187,002) in North America. There are 17,712 (95% Confidence Interval: 7,590 to 32,691) new transcatheter aortic valve replacement candidates in the European countries and 9,189 (95% confidence interval: 3,898 to 16,682) in North America (4) every year.

Peri-procedural stroke is associated with increased morbidity and mortality after both surgical and transcatheter aortic valve replacement (17). Despite the development of new-generation transcatheter aortic valve replacement devices and enhanced operator skills, stroke remains one of the most concerning complication of these procedures (18, 19). Although the etiology of strokes during transcatheter or surgical aortic valve replacement is multifactorial, the dominant etiology are intra-procedure embolic events (20). A study with transcranial Doppler ultrasound during transcatheter aortic valve replacement demonstrated that majority of intra-procedural embolic events occurred during balloon valvuloplasty, delivery of the prosthetic stent-valve, manipulation of catheter across the aortic valve, and valve implantation (21). Emboli were detected with transcranial Doppler ultrasound during surgical aortic valve replacement was mainly seen during insertion of an aortic cannula at the start of cardiopulmonary bypass and immediately after the release of the aortic clamp and in connection with the de-airing procedures (22). The overall rate of stroke for isolated surgical aortic valve replacement in the global United States population is approximately 1.5% based on the Society of Thoracic Surgeons (STS) database (23, 24). Most of strokes post transcatheter aortic valve replacement are in early post procedure period. The proportion of patients who experience stroke ranges between 3-6% after transcatheter aortic valve replacement, 45% of the events occur within first 2 days; 28% between 3 and 10 days; 4% between 10 and 30 days; and 10.5% of strokes occurs from 1 months to 2 years (25).

METHODS

We performed a narrative literature review to the current literature on risk factors and prevention of stroke peri-procedure. We searched the PubMed, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), and Cumulative Index to Nursing and Allied Health Literature (CINAHL) databases with no restrictions on language. Key words of transcatheter aortic valve replacement, surgical aortic valve replacement, stroke, cerebrovascular event, cerebral protection devices and mortality were utilized. Metanalysis, large prospective studies and systematic reviews were included if published before March 31st 2020. We hand-searched the reference lists of included articles and relevant reviews to identify additional articles.

RESULTS

Predictors of stroke

Stroke is a potential complication of treating patients with aortic stenosis using surgical, transcatheter aortic valve replacement and balloon valvuloplasty (21). The risk of strokes during follow-up after stent less aortic valve replacement is related to the individual risk factors of the patients rather than to the valve prosthesis itself (25). To eliminate discrepancies, the Valve Academic Research Consortium has determined a set of standardized stroke-related definitions (that have been utilized since their publication (26).

TERM	DEFINITION
Stroke	Duration of a focal or global neurological deficit >24 h; OR <24 h if available neuroimaging documents a new hemorrhage or infarct; OR the neurological deficit results in death
Transient Ischemic Attack	Duration of a focal or global neurological deficit <24 h, any variable neuroimaging does not demonstrate a new hemorrhage or infarct
Ischemic Stroke	An acute episode of focal cerebral, spinal, or retinal dysfunction caused by infarction of the central nervous system tissue
Hemorrhagic Stroke	An acute episode of focal or global cerebral or spinal dysfunction caused by intraparenchymal, intraventricular, or subarachnoid hemorrhage

Analysis of a registry sponsored by the National Institutes of Health reporting upon 360,437 patients who underwent surgical aortic valve replacement from 1998 to 2011 identified patients who experienced stroke were more likely to be women, older, higher Elixhauser comorbidity risk scores, and had higher rates of heart failure, carotid stenosis, renal failure, weight loss, anemia, preoperative arrythmias, prior paralysis or neurological dysfunction. The study showed that post-operative stroke after isolated surgical aortic valve replacement occurred in 1.4% of the patients. When stratified by surgical risk, the overall incidence of stroke in low- (Edinburgh Cardiac Surgery Score <0–5), medium- (score <6–15), and high-risk (score >16+) patients was 0.8%, 2.3%, and 5.4%, respectively (27). Paradoxically, patients with stroke were less likely to have peripheral vascular disease, diabetes mellitus, obesity or depression (27). No difference was found by race/ethnicity, hospital teaching status, hospital bed or region (27) although high volume centers had lower incidence of ischemic stroke compared to low medium volume centers (27). The incidence of stroke post transcatheter aortic

valve replacement was 9%, and more than half occurred >24 hours after the procedure. The onset of symptoms was early (≤24 hours) in 42% (n = 8), and delayed (>24 hours) in 58% (n = 11) of patients. Computed tomography (CT) imaging showed cortical infarct in 8 patients (42%), a lacunar infarct in 5 (26%), intracerebral hemorrhage in 1 (5%), and no abnormalities in 5 (26%) of the patients (36). A meta-analysis demonstrated that the 30-day stroke incidence was 5.5% in the high-risk group, 6.7% in the inoperable patient cohort, and 3.2% in a weighted meta-analysis of 3519 transcatheter aortic valve replacement patients (7, 28, 29).

Extensive calcification of the ascending aorta has been associated with increased risk of stroke after surgical aortic valve replacement. A study reported strokes occurred in 4% of 25 patients with a "porcelain aorta" (Heavy circumferential calcification or severe atheromatous plaques of the entire ascending aorta extending to the arch such that aortic cross-clamping is not feasible) undergoing aortic valve surgery using a no-clamp technique (30). Another study reported a 10% risk of stroke in 62 patients with extensive calcification of the ascending aorta who underwent surgical aortic valve replacement. The risk differed based on the different management strategies of the ascending aorta (31). Multiple studies on transcatheter aortic valve replacement have identified peri-operative risk factors for stroke: increasing age (19), female gender, diabetes mellitus, bypass procedure time >120 min, calcification of ascending aorta, left ventricular ejection fraction <40%, acute kidney injury, peripheral vascular disease, history of ischemic stroke, walking < 300 meters during 6 minute walk test, carotid stenosis, balloon post-dilation, valve embolization/ dislodgment and emergency department admission (32, 33, 34, 35, 36). Studies have shown discrepant results about atrial fibrillation as a predictor, although majority of studies showed an increased risk of stroke (37), particularly with new onset periprocedural atrial fibrillation (19, 37, 38). History of chronic atrial fibrillation increases the risk for late stroke after procedure (19). One study reported that atrial fibrillation was not an independent risk for early stroke but was a predictor of poor survival (26). Currently there are no clear guidelines on anticoagulation therapy after short episodes of post procedural atrial fibrillation (38). However, patients undergoing transcatheter aortic valve replacement are at high risk for thromboembolism and especially in patients with history of atrial arrhythmia, a more aggressive antithrombotic treatment should be the considered (35). Low ejection fraction has also been identified as an independent risk factor for strokes (20, 27, 39, 40).

Different accesses are used to perform transcatheter aortic valve replacement either using transfemoral, transapical, subclavian and transaortic approaches. Non-femoral access is only used in 6% to 10% of patients undergoing the procedure in the United States. Transfemoral access for transcatheter aortic valve replacement involves the advancement of a delivery catheter containing the valve from the common femoral artery to the ascending aorta in a retrograde fashion (41), whereas transapical access for transcatheter aortic valve replacement is more invasive and requires a left anterolateral thoracotomy. Transfemoral access is the preferred approach for transcatheter aortic valve replacement, given less inherent risk for periprocedural complications by avoiding mini-thoracotomy and left ventricular puncture (42). There is some data that supports that the stroke rate for transfemoral maybe higher than for transapical approach, probably because of the passage of 22 French or 24 French catheters around the aortic arch (43). Similarly, other studies have reported a reduced risk of cerebral embolism during transapical implantation compared to the trans-femoral approach (44) presumably by avoiding manipulation of large sized catheters across the aortic arch and thereby potentially reducing the risk of embolization of aortic atheroma to the brain (45). Patients that are not candidates for transfemoral access may have an increased risk for late stroke (46) which is consistent with the finding of increased risk of stroke seen in patients with peripheral vascular disease (19).

There is controversy regarding whether transfemoral approach is associated with an increased stroke rate (19, 43, 47). In a recent multicenter study conducted in Europe, 882 patients who underwent transfemoral and transapical transcatheter aortic valve replacement approaches were compared. Both approaches had similar stroke rates within 30 days, even after adjustment for baseline differences (odds ratio: 0.87, 95% confidence interval: 0.11-7.49, p = 0.91). However, the transapical access appeared to be a predictive factor for new onset atrial fibrillation which may affect the risk of acute and subacute stroke. Other reports that the stroke rates are similar with transfemoral and transapical approaches, ranging from 2-3% for transfemoral and 1-5% for transapical approaches, respectively, without any statistically significant difference (48, 49, 50). Recent studies have found no statistically significant difference in stroke rate with transapical compared with transfemoral transcatheter aortic valve replacement techniques (46, 47). In a multicenter study, two third of the 60 patients undergoing transfemoral compared to transapical transcatheter aortic valve replacement had new ischemic lesions identified using diffusion weighted magnetic resonance imaging (baseline and within 6 days) but no differences were identified between the two access groups (51). Most patients (76% of 60 patients) had multiple lesions, with a median number of lesions being 3 (range 1–31). According to data in the Society of Thoracic Surgeons in the Transcatheter Valve Therapy Registry (52), 5.7% of patients underwent non-transfemoral access (transaxillary access in 34.4% of the non-transfemoral approaches) for the placement of Edward-SAPIEN[BC1] 3 valve.. After propensity matching, transaxillary access had lower 30-day mortality (5.3% vs. 8.4%; p < 0.01), shorter lengths of intensive care unit and hospital stay, but a higher stroke rate (6.3% vs. 3.1%; p < 0.05) compared with transapical and transaortic approaches. Nonetheless, the evaluation of stroke and vascular complications were not centrally adjudicated and might have been under-reported in this analysis (53).

On the other hand, the outcomes of patients from the Medtronic-CoreValve United States Pivotal Trial Program who underwent subclavian/transaxillary access were analyzed through propensity matching to those with transfemoral access (54). There was no difference in the composite endpoint of all-cause mortality or major stroke

between the groups. Similarly, there was no difference in the rate of stroke at 1 year (9.9 vs 7.6, p = 0.364). Overall, major morbidity and mortality rates using subclavian/axillary artery for transcatheter aortic valve replacement were equivalent to transfemoral- transcatheter aortic valve replacement. The authors suggested that the subclavian/transaxillary artery access should be the preferred secondary access site for transcatheter aortic valve replacement (50).

Randomized trials comparing surgical and transcatheter aortic valve replacement

In Placement of Aortic Transcatheter Valves (PARTNER) trial, using the balloon expandable Edward-Sapiens valve, the rates of major stroke were 3.8% in the transcatheter group and 2.1% in the surgical aortic valve replacement group at 30 days (p = 0.20) and 5.1% and 2.4%, respectively, at 1 year (p = 0.07) (54). Similarly, transcatheter aortic valve replacement was associated with a higher risk of stroke in the Placement of Aortic Transcatheter Valves cohort B when compared with inoperable patients treated without aortic valve replacement (55). Thirty-day stroke rate (5.1% vs. 3.7%; p = 0.09) was similar, but 30-day major stroke rate (3.9% vs. 2.2%; p = 0.018) was lower after transfemoral-transcatheter aortic valve replacement than surgical aortic valve replacement. In both groups, risk of stroke was highest in the first post-procedure day, followed by a near-constant low-level risk upto 48 months. Major stroke was associated with a decline in quality of life at 1 year in both surgical aortic valve replacement and transcatheter aortic valve replacement (56).

In a randomized trial using the self-expandable Medtronic-CoreValve bioprosthesis (57) out of 747 patients with high surgical risk (mean Society of Thoracic Surgery score 7.4%) who either underwent either transcatheter aortic valve replacement or surgical aortic valve replacement. Patients treated with transcatheter aortic valve replacement (83% treated using iliofemoral access) had a lower stroke incidence at 30 days and 1 year. In comparison to the (Placement of Aortic Transcatheter Valves) trial, stroke incidence in the Medtronic-CoreValve trial was similar in transcatheter aortic valve replacement patients (35) but occurred at a 3-fold higher rate in the surgical aortic valve replacement group.

In Placement of Aortic Transcatheter Valves 2 trial (intermediate-risk patients), the results were similar between the two groups. At 2 years, the rate of disabling stroke was 6.2% after transcatheter aortic valve replacement and 6.4% after surgical aortic valve replacement. Earlier outcomes at 30 days and 1 year similarly showed no significant differences between transcatheter aortic valve replacement and surgical aortic valve replacement with respect to stroke occurrence (13). In PARTNER-3 (Placement of Aortic Transcatheter Valves) trial (low surgical risk patients) the Kaplan–Meier estimate for stroke occurrence at 1-year was 1.2% in the transcatheter aortic valve replacement group compared with 3.1% in the surgical aortic valve replacement group (hazard ratio 0.38; 95% confidence interval 0.15-1.00) (58). Half of the strokes occurred within 48 hours after the procedure (36, 59). Nonetheless, the risk of stroke was high (5.5% after 30 days) in transfemoral transcatheter aortic valve replacement patients treated in the randomized Placement of Aortic Transcatheter Valves 2 trial (2).

Outcomes of stroke

A large study on surgical aortic valve replacement revealed that in-hospital mortality for patients with stroke was 23.8% compared with 4.6% in those without stroke. Patients with post-operative stroke also had increased hospital length of stay, gastrointestinal complications, systemic infection, and respiratory failure (32). Post-operative stroke with permanent disability was a strong predictor of 30-day mortality after aortic valve replacement in octogenarian patients (60).

Histopathology of debris

Multiple embolic protection devices have been used to capture debris during transcatheter aortic valve replacement procedure. Study of analyzed debris captured using the Sentinel dual-filter embolic protection device showed that the captured embolic material had components of (in decreasing frequency): acute platelet rich thrombus in the presence of other tissue (99%), followed by arterial wall (84%), fibroelastic tissue consistent with valve tissue (84%), calcifications (58%), foreign material (33%), myocardial fibers (14%), necrotic core (12%), and organizing thrombus (7%). Acute thrombus without any associated debris was identified in <1% of cases. The histopathology of embolic debris was similar to that observed in Boston Scientific-LOTUS vs Medtronic-Core Valve Evolut vs Edward-SAPIEN 3 [BC2] (61). Histomorphology showed captured debris from patients treated with the Boston Scientific-Lotus valve was significantly smaller in total tissue area. In contrast, the number of patients with large tissue particles was highest with the Edward-SAPIEN 3 valve trial. The frequency of tissue embolization during transcatheter aortic valve replacement was higher with balloon expandable transcatheter heart valve compared with self-expanding valves (79% vs. 56%; p = 0.05) (61, 62).

Cerebral protection devices

Even clinically “silent” brain infarctions seen on magnetic resonance imaging are associated with neurocognitive deficits (63, 64, 65, 66) and can occur in as many of 80% of patients after transcatheter aortic valve replacement (68, 68, 69, 70). The first data on cerebral embolic protection devices demonstrated a reduction in number and volume of new ischemic brain lesions on diffusion-weighted Magnetic Resonance Imaging and a trend toward lower rates of neurocognitive deficits compared with procedures without cerebral protection devices (71, 72, 73, 74, 75).

Cerebral embolic protection devices (EPDs) are currently available as distal filters. The TriGuard HDH embolic deflection device (Keystone Heart Ltd., Caesarea, IL, USA) is delivered transfemorally via a 9 French Mullins introducer sheath and deploys a single mesh filter with 130-μm pores across the ostia of all three supra-aortic vessels. These devices demonstrated a reduced risk of stroke in patients undergoing transcatheter aortic valve procedures (76). TriGuard

TABLE 1: RCT's evaluating risk of stroke and TAVR.

Author	Study	Type of study (number of patients)	Conclusion
Leon, 2017	PARTNER 1 Cohort A	RCT (699)	The risk of stroke or transient ischemic attack at 2 years is 11.2% in the TAVR group.
Leon, 2017	PARTNER 1 Cohort B	RCT (699)	The risk of minor stroke at 2 years is 13.8% in the TAVR group.
Leon, 2018	PARTNER 2	RCT (365).	At 2 years, the rate of disabling stroke was 6.2% in TAVR group.
Mack, 2020	PARTNER 3	RCT (1000)	The risk of stroke after TAVR at 1 year was 1.2%.
Adams, 2014	TAVR with a self-expanding Prosthesis	RCT (747)	8.8% of patient were diagnosed with stroke by 1 year after TAVR with a self-expanding transcatheter aortic-valve bio prosthesis.
Kleiman, 2016	Neurological Events following TAVR and predictors-CORE VALVE Trials	Prospective Registry (3687)	The 1-year stroke rate after TAVR was 8.4%
Kodali, 2016	Outcomes after SAPIEN 3 transcatheter aortic valve replacement in inoperable, high-risk and intermediate-risk patients with aortic stenosis	Prospective Registry (1661)	The rate of stroke was 5.3% at 30 days, SAPIEN 3 transcatheter heart valve associated with lower rates of stroke.
Walters, 2013	The SOURCE ANZ Registry	Prospective Study (132)	The Risk of stroke at 1 year was found to be 3.2%, no significant difference noted between TF vs TA approach.
Yamamoto, 2016	OCEAN-TAVI Registry	Prospective Study (1215)	The rate of disabling stroke at 30 days was 1.8% in the study population who underwent TAVR.
Auffret, 2017	Temporal Trends in TAVR in France: FRANCE 2 to FRANCE TAVI	Prospective Registry (16969)	Stroke rate was found to be at 2.0% at 30 days after TAVR.
Walther, 2015	GARY Registry	Prospective Registry (15964)	Stroke occurred in total of 1.5% of patients after TAVR.
Thomas, 2010	SOURCE Registry	RCT (1038)	Stroke was noted as post-procedure complication in 2.5% at 30 days, no difference of stroke noted between TF, TA approach.
Mario, 2012	The 2011-12 pilot European Sentinel Registry of TAVI	Prospective Study (4571)	1.8% of patients are noted to have stroke as In-hospital complication after TAVR.
Schymik, 2014	SOURCE XT Registry	Prospective Study (2688)	The procedure-related stroke rate was observed in 2.0% of patients, 3.6% & 6.3% had stroke 30 days, 1 year post TAVR.
Moat, 2011	U.K. TAVI Registry	Prospective study (870)	The Incidence of stroke was 4.1% 30 days post TAVR.

TAVR - Transcatheter Aortic-Valve Replacement, TF = transfemoral, TA = transapical, TAVI - Transcatheter Aortic-Valve Implantation, PARTNER - Placement of Aortic Transcatheter Valves, RCT - Randomized Controlled Trial, SOURCE - SAPIEN Aortic Bioprosthesis European Outcome, ANZ - Australian and New Zealand, OCEAN - Optimized CathEter vAlvular iNtervention, FRANCE 2 - French Aortic National CoreValve and Edwards-2, GARY - German Aortic Valve Registry, SOURCE XT - Edwards SAPIEN XT Aortic Bioprosthesis Multi-Region Outcome Registry, U.K – United Kingdom.

TABLE 2: Schematic / steps of transfemoral TAVR And EPD delivery[1,2]	
1	Ultrasound guided access of the femoral artery for transfemoral-TAVR.
2	Insertion of the TAVR Delivery sheath. Intravenous unfractionated heparin is then administered to achieve an activated clotting time > 250 seconds
3	Sentinel Device Inserted through a 6French sheath via right radial or brachial artery
4	Positioning of the proximal polyurethane filter in the brachiocephalic trunk
5	Delivery of the second filter to the left common carotid artery
6	A 6-Fr AL-1 catheter is passed through the valve delivery sheath over a 145-150 cm 0.035-inch J tipped guidewire, and exchanged for a straight-tip wire to cross the valve
7	Once across, the straight-tip wire is exchanged for a 300-cm J-tipped wire
8	The AL-1 catheter is then removed and exchanged for a 6-Fr angled pigtail catheter
9	Both catheters are then connected to manometry, and peak left ventricular, and aortic systolic and diastolic pressures measured
10	A preshaped stiff guidewire is then placed through the angled pigtail catheter into the left ventricle, with the transition point of the guidewire held above the apex and pointing away from the ventricular wall
11	Once the valve delivery system is brought into appropriate implanting position (targeting an implant depth of 3-5 mm). The system is allowed to align itself within the native aortic annulus, and maintain contact with the top of the aortic arch for maximum stability
12	The first 1/3 of the bio prosthesis is deployed by very slow counterclockwise rotation of the actuator, in short increments in the direction of the marked arrows
13	If the operator is satisfied with the valve position at annular contact, valve is continually deployed until just before the "point of no recapture
14	If the implanting team is satisfied with valve position and performance, tension in the system is released just before full deployment to reduce potential for valve movement by retracting the guidewire, slight forward pushing on the delivery system, and turning the deployment knob very slowly to detach the paddles one at a time
15	The system is locked in the descending aorta by activating the deployment knob trigger, and retracting the grey hand rest to the blue deployment knob ("grey to blue"). The system is removed over the stiff wire.
16	A final angiogram is performed after pullback of the angled pigtail catheter for assessment of valve placement and paravalvular leak
17	The large sheath is then removed over a J-tipped guidewire, ProGlide® deployed, and protamine administered.

EPD= embolic protection device, TAVR = Transcatheter Aortic-Valve Replacement, TF = transfemoral.

[1] Kalra, A., Reardon, M., Barker, C., Kleiman, N. and Reyes, M., Step-by-step guide: transfemoral Corevalve Evolut TAVR.
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deflection device also has clinical data from the DEFLECT (A Prospective, Randomized Evaluation of the TriGuard™ HDH Embolic Deflection Device During transcatheter aortic valve replacement in phase I to III trials showing safety and efficacy in smaller trials outside of the United States- use of TriGuard cerebral protection during Transcatheter Aortic Valve Implantation achieved a complete cerebral protection in 89% of patients, and appears to mitigate new neurologic deficits and cognitive decline at discharge and 30 days (71, 72).

The Claret Sentinel device (Claret Medical Inc., Santa Rosa, California, USA) consists of a dual-filter system inserted through a 6 French sheath inserted via right arm access. The proximal component, a radiopaque nitinol frame with a 140-µm pore polyurethane filter, is deployed in the brachiocephalic and a second filter is positioned across the left common carotid artery ostium, both are withdrawn into the catheter and removed after transcatheter aortic valve replacement. Sentinel Cerebral Protection System has a smaller catheter for delivery than the TriGuard and Embol-X systems (9Fr and 24Fr, respectively) (77). This device protects the right vertebral, right carotid, and left carotid arteries from embolization but not the left vertebral (61, 78). The SENTINEL(Protection Against Cerebral Embolism During Transcatheter Aortic Valve Replacement) trial recruited 363 patients from 19 centers and use of Embolic Protection Device was associated with a 38% reduction in all strokes at 30 days compared with procedures performed without Embolic Protection Device albeit did not reach statistical significance. There was a 42% (non-significant) reduction in ischemic lesions identified on diffusion weighted magnetic resonance imaging performed between 2 and 7 days in the Embolic Protection Device arm compared with procedures performed without Embolic Protection Device (79). Total procedure time was increased by approximately 13 min, and fluoroscopy time was increased by 3 min with use of Embolic Protection Device. The United States Food and Drug Administration (FDA) has cleared the Sentinel Cerebral Protection System (Claret Medical) for use during transcatheter aortic valve replacement procedures to reduce the risk of stroke caused by embolic debris in June 2017 (80).

A study of Sentinel Cerebral Embolic Protection Device during transcatheter aortic valve replacement showed improvement in stroke-free survival with estimated survival of 2.1% versus 6.8% in the group without Embolic Protection Device (p = 0.01; odds ratio 0.30; 95% confidence interval 0.12-0.77; absolute risk reduction 4.7%; number needed to treat of 21) (80). The use of Sentinel cerebral embolic protection device was associated with reduced rate of disabling and nondisabling stroke(Combined) from 4.6% to 1.4% (p = 0.03; Odds Ratio: 0.29; number needed to treat 31) compared with patients undergoing the procedure without EPD (85) The MISTRAL-C(randomized MRI Investigation in TAVI with Claret) trial, using the Claret Sentinel device randomized 65 patients, and identified a significant reduction in ischemic lesions on diffusion weighted magnetic resonance imaging performed between 2 and 7 days in the Embolic Protection Device group compared with procedures performed without Embolic Protection Device (20% versus 0%) (81). CLEAN-TAVI (Claret Embolic Protection and TAVI) trial demonstrated a reduction in number (5 vs. 10; p = 0.009) and volume of new ischemic lesions (205 mm3 vs. 472 mm3; p = 0.009) on diffusion-weighted magnetic resonance imaging following transcatheter aortic valve replacement with use of the Claret Sentinel filter-based embolic protection device (74).

One meta-analysis including only patients treated in randomized trials, with the Claret dual filter, Triguard, Claret Sentinel and Claret Embol-X devices, (n = 643) showed that EPDs were safe and associated with reduction in stroke and death (82). Similarly, Sentinel Cerebral Protection System use in transcatheter aortic valve replacement was associated with lower rates of 30-day mortality [0.8% vs 2.7%; relative risk 0.34 (95% confidence interval 0.12-0.92)], 30-day symptomatic stroke [3.5% vs 6.1%; relative risk 0.51 (95% confidence interval 0.29-0.90)] and major or life-threatening bleeding events [3.3% vs 6.6%; relative risk 0.50 (0.26-0.98)] (83). Another metanalysis including 3 registries and 5 randomized trials (n = 1285) showed that Embolic protection Device use was not associated with a reduced rate of mortality and new ischemic cerebral lesions on diffusion weighted magnetic resonance imaging. The use of Embolic protection Devices during transcatheter aortic valve replacement seemed to be associated with a lower 30-day stroke rate, although this result is driven by a single nonrandomized study. Overall, the use of cerebral embolic protection devices is associated with a smaller volume of ischemic lesions, and smaller total volume of ischemic lesions on diffusion weighted magnetic resonance imaging (84).

CONCLUSION

Aortic stenosis is the most common valvular heart disease and it is expected to increase with aging population. Ischemic stroke is a complication that can be seen after transcatheter aortic valve replacement and adversely affects the rates of death and disability after transcatheter aortic valve replacement. Strategies such as subclavian/transaxillary artery access when transfemoral approach is not possible and use of Embolic Protection Devices such as Food and Drug Administration approved Sentinel Cerebral Embolic Protection may reduce the rates of ischemic stroke during transcatheter aortic valve replacement.

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