Impact of Complications During Transfemoral Transcatheter Aortic Valve Replacement: How Can They Be Avoided and Managed?

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Transcatheter aortic valve replacement (TAVR) has revolutionized the treatment of aortic stenosis and is the treatment of choice for patients at prohibitive and high surgical risk. Extension of indications into intermediate surgical risk has begun, and recently 2 large randomized trials demonstrated that TAVR may be superior to surgery in patients at low surgical risk and can potentially offer better results at initial follow-up.[1–3] TAVR practice has evolved continuously with concomitant simplification of the procedure. If one disregards the financial considerations, predictability of the procedural outcome and certainty regarding the durability of TAVR prostheses are 2 of the main remaining restrictions to universal implementation.

Transfemoral access is the preferred approach, as it has a 20% relative reduction in mortality compared with surgical aortic valve replacement (SAVR) (hazard ratio HR, 0.80; 95% CI, 0.69–0.93; P=0.024).[3] Understanding the mechanisms that underlie complications during transfemoral TAVR is essential, and familiarity with the techniques for their prevention and treatment is mandatory. In this review, we provide a state-of-the-art overview on the avoidable procedural complications of contemporary transfemoral TAVR practice, with a specific focus on strategies for their prevention and management.

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Vascular Access Complications

Prevention, early identification and effective management of vascular access complications remain an important aspect of managing patients undergoing TAVR. The incidence of vascular complications has varied according to the definition that has been applied. In patients receiving first-generation valves, ≈12% of patients experienced a major vascular complication and 16% a life-threatening bleed, as defined by the Valve Academic Research Consortium criteria.[4] Over time, there has been a significant reduction in major vascular complications, with an incidence of 6% to 8% in recent TAVR trials.[5–7] This reduction has been driven by a combination of smaller sheath sizes, flexible delivery systems, multidetector computed tomography (MDCT) assessment of the peripheral vasculature, and operator experience.[8,9] However, vascular complications and hemorrhage remain a significant challenge in contemporary practice and are associated with increased length of stay and higher mortality at 1 year (HR, 2.31; 95% CI, 1.20–4.43; P=0.012).[6,10,11]

The contemporary Valve Academic Research Consortium-2 criteria include aortic and peripheral access complications within the category of major vascular complications.[12] This category comprises aortic/annular dissection or rupture, ventricular perforation, and pseudoaneurysm or aneurysm. Major access complications include vascular injury (dissection, stenosis, perforation, rupture, fistula, pseudoaneurysm, hematoma, irreversible nerve injury, compartment syndrome, closure device failure), or a requirement for unplanned surgical/endovascular intervention leading to death, life-threatening or major bleeding, visceral ischemia, or neurological impairment. The Valve Academic Research Consortium-2 also includes distal embolization resulting in amputation or irreversible end-organ damage, and any significant ipsilateral lower extremity ischemia or access-site nerve injury (Table S1).

Vascular complications most commonly occur at the access site, and bleeding and/or hematoma formation occurs most frequently. Interestingly, studies consistently show that failure of a closure device (adopted to prevent vascular access complication) is the most common cause of a major vascular complication.[13,14]

A number of patient- and procedural-related risk factors have been identified. Patient-related factors include vascular calcification (especially when circumferential), preexisting peripheral vascular disease, and female sex.[11,13] Procedural-related risk factors include larger sheath sizes, increased sheath:femoral artery ratio, and operator inexperience.[14,15]

Complications involving the femoral segment are more common than those involving the iliac segment, with dissection being more frequent than rupture.[13] In larger series of patients undergoing TAVR, ileofemoral dissection has been reported in ≈6.5% of patients and rupture in ≈3% to 5%.[16,17] Pseudoaneurysm, embolization, occlusion, and access site infection are uncommon.

How to Avoid

Avoidance of vascular complications begins with meticulous MDCT assessment of the peripheral vessels (Figure 1). The role of MDCT is to assess the minimal luminal diameter and identify heavy (>270°) calcification or calcification at the site of probable puncture, the position of the femoral bifurcation relative to the femoral head, and any significant vascular pathology.[18] In patients with significant anterior calcification or deep femoral arteries, surgical cutdown may be preferable to percutaneous access to avoid the increased risk of vascular closure device failure. When transfemoral access is not feasible, MDCT is the modality of choice to assess suitability for subclavian access or to determine the location of "calcium-free windows" in the descending aortic wall if transcaval access is being considered.

Several intraprocedural techniques have emerged to reduce vascular access complications. The use of real-time ultrasound guidance to puncture the common femoral artery has become commonplace. Ultrasound reduces the incidence of vascular complications during cardiac catheterization[19] and was associated with reduced vascular complications in patients undergoing TAVR in a single-center retrospective cohort.[20] Fluoroscopy can be used to facilitate femoral puncture, using a radiopaque marker to "label" the position of the femoral head or digital subtraction angiography to puncture the vessel in real time. An alternative approach is to "road-map" the common femoral artery after performing an angiogram from the contralateral access site. Use of a micropuncture kit (Cook Medical, Bloomington, IN) to confirm the position of the puncture prior to upsizing the sheath is an intuitive strategy to minimize trauma before passage of a large catheter at an unfavorable common femoral artery site.

Recently, an integrated technique involving (1) angiographic assessment of the iliac-femoral axis via secondary access, (2) a J-tip 0.035-inch guidewire placed as reference in the ideal femoral artery spot (above the bifurcation), and (3) ultrasound imaging to identify the J-tip of the 0.035-inch guidewire and guide the femoral puncture has been proposed[21] (Figure 2). Another novel technique in heavily calcified iliofemoral vessels is the use of intravascular lithotripsy to facilitate transfemoral access by disrupting intimal and medial calcification and increasing vascular compliance via controlled microfractures and microdissections. This technology has been tested in patients with calcific femoropopliteal vascular lesions in the DISRUPT-PAD (Shockwave Medical Peripheral Lithoplasty System Study for Peripheral Artery Disease) I and DISRUPT-PAD II studies.[22,23] Interestingly, the incidence of vascular complications was low in these studies, with only 1 (1.7%) wire-related dissection requiring stent placement. Notably, no embolic debris was present when distal embolic filters were used, suggesting a low risk of distal embolization.[23]

Recently, in a registry of 42 patients with iliofemoral vascular disease considered prohibitive for transfemoral access undergoing TAVR, intravascular lithotripsy allowed femoral access and safe delivery system passage in >90% of the cases.[24,25] In this experience, no iliofemoral perforation or dissection requiring stent implantation was observed, and only 1 (2.4%) patient developed pseudoaneurysm and 1 (2.4%) required endarterectomy.[25]

Novel vascular closure devices, such as the MANTA (Teleflex, Wayne, PA) collagen-plug device, may reduce the rate of closure failure but await evaluation in head-to-head studies against current suture-based closure devices (eg, ProStarXL and Perclose ProGlide; Abbott Vascular, Abbott Park, IL).[26]

How to Manage

Optimal management of vascular complications relies on early recognition. Routine crossover angiography to assess for aortic/iliofemoral dissection or perforation after sheath removal is current standard practice, and placement of a crossover wire from the contralateral femoral artery allows rapid vascular access if required. Transradial secondary access has recently been demonstrated to be suitable for the management of peripheral vascular complications during TAVR and may reduce the rate of secondary femoral access site complications.[27,28]

Limited dissection or perforation may be successfully managed by prolonged occlusive balloon inflation. Percutaneous deployment of a covered stent or surgical repair is indicated for more extensive dissection or bleeding (especially if there is associated cardiovascular instability or threatened/actual limb compromise) and is associated with good long-term outcome.[29] Stenting is usually preferred to surgical repair when the injury is above the inguinal ligament.

Device Landing Zone Rupture

Device landing zone rupture is a rare but feared complication of TAVR, with an overall mortality up to 48% and can be as high

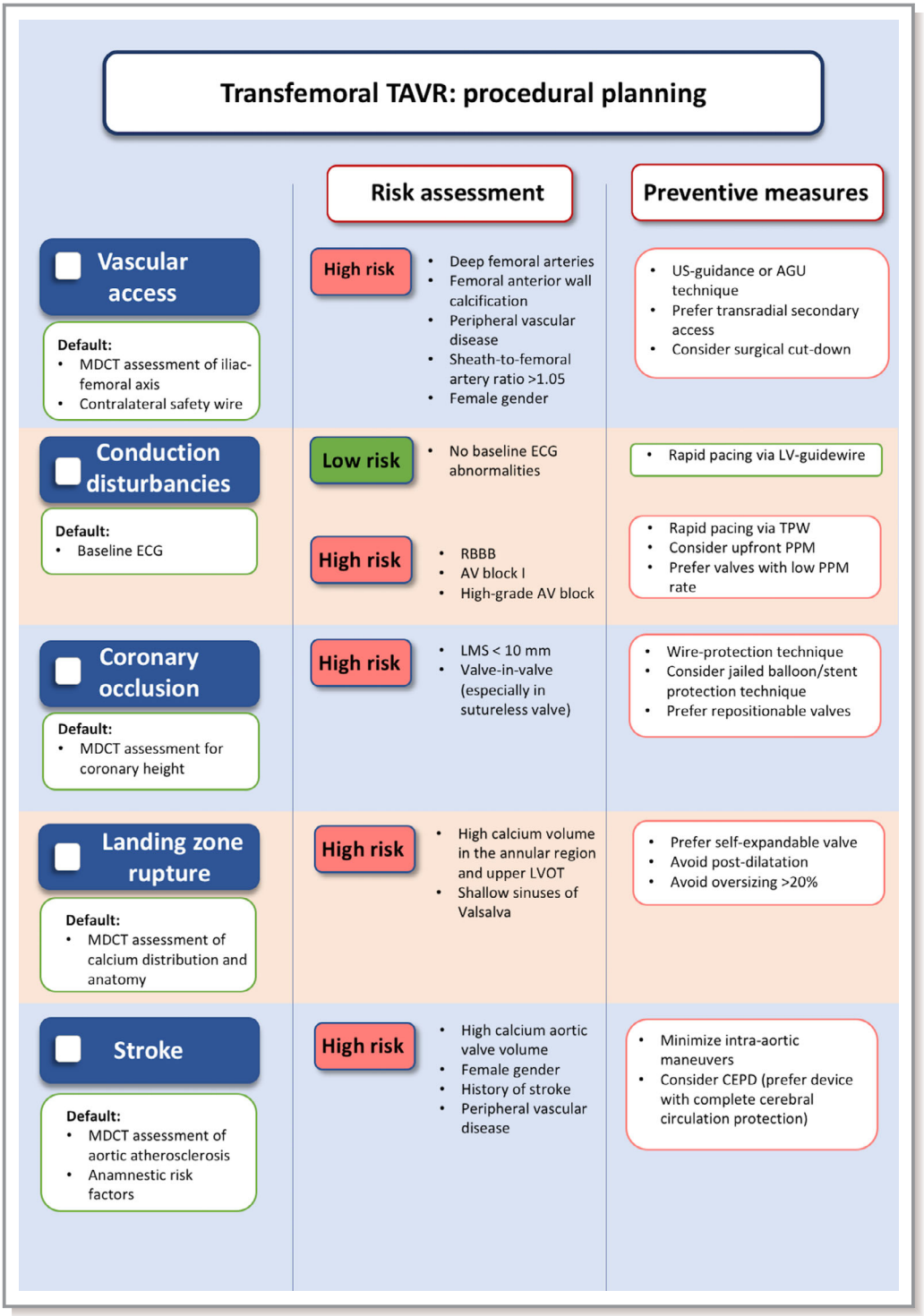


Figure 1. Checklist of avoidable procedural complications as part of the procedural planning for TAVR. AGU indicates angiographic, guidewire, and ultrasound; CEPD, cerebral embolic protection device; LMS, left main stem; LV, left ventricular; LVOT, left ventricular outflow tract; MDCT, multidetector computed tomography; PPM, permanent pacemaker; RBBB, right bundle branch block; TAVR, transcatheter aortic valve replacement; TPW, temporary pacing wire.

as 75% in cases of uncontained rupture.[30] Overall, landing zone ruptures account for 7% of all the cases of emergent conversion to surgery during TAVR.[31] The reported incidence of landing zone rupture is up to 0.5% to 1% of all TAVR procedures,[5,30,32–34] although the real incidence might be higher when cases with delayed presentation are accounted for.[35]

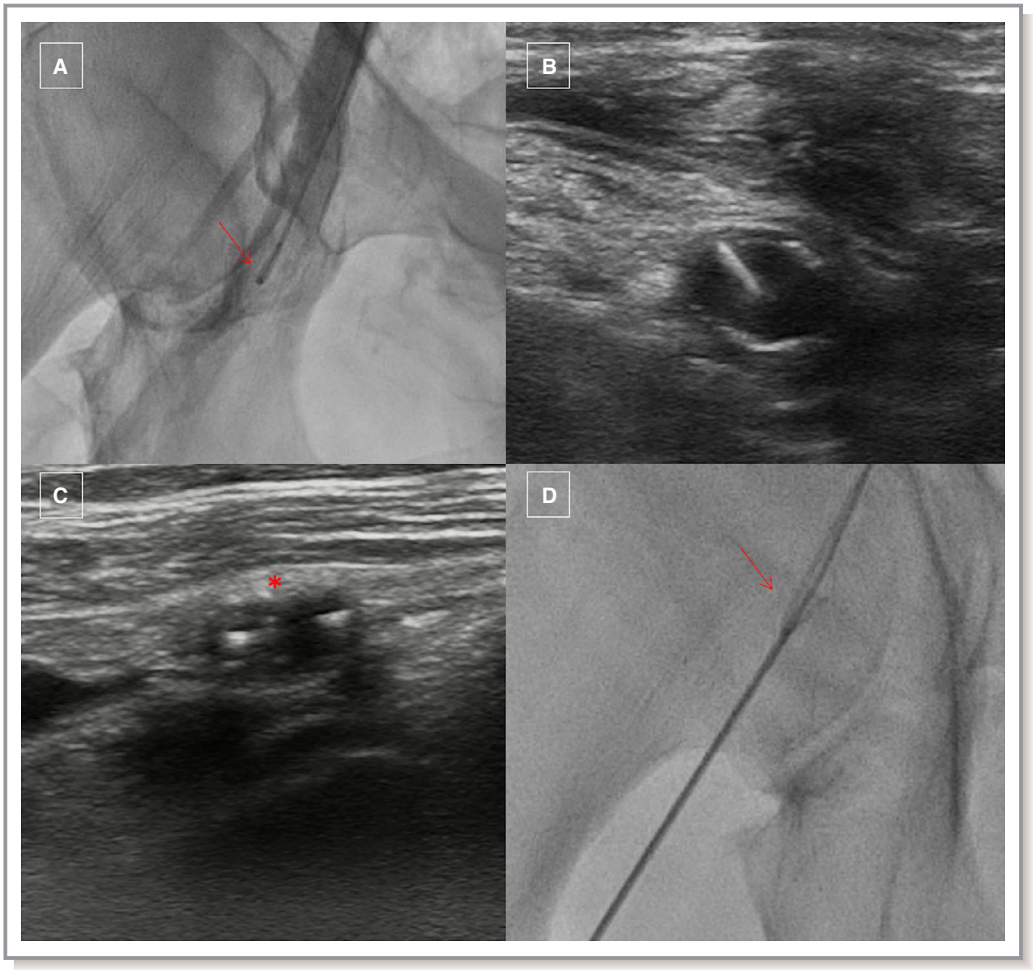


Figure 2. The angiographic, guidewire, and ultrasound (AGU) technique for vascular management. The J tip of the 0.035-inch guidewire is placed, under fluoroscopic guidance, in the ideal femoral artery spot (above the bifurcation) (**A**). The J tip of the 0.035-inch is identified using ultrasound imaging (**B**). The femoral artery puncture is performed under ultrasound guidance. The asterisk indicates the needle penetrating the anterior wall of the femoral artery (**C**). Site of sheath insertion (**D**).

The most frequent anatomic site of rupture is the aortic annulus (involved in two thirds of cases), although left ventricular outflow tract (LVOT, 10%), sinus of Valsalva (16%), and sinotubular junction (6%) rupture have also been described.[30] Self-expanding systems have rarely been associated with aortic root rupture (unless valve balloon postdilatation is performed) and landing zone rupture is usually related to use of a balloon-expandable device.[36]

How to Avoid

Meticulous procedural planning using preprocedural imaging with MDCT and 3-dimensional reconstruction is essential to minimize the risk of landing zone rupture. Both anatomic and procedural variables are associated, but a high burden of LVOT/subannular calcification is recognized as the most important predictor. Notably, in a large multicenter TAVR cohort, the calcium score was significantly increased in patients who experienced landing zone rupture compared with other patients (181±211 versus 22±37; $P<0.001$).[30]

Perhaps more important than the calcific burden is the distribution of calcium. In particular, a higher calcium volume in the upper LVOT (but not in the aortic valve region) has been associated with the risk of landing zone rupture.[37] Notably, Barbanti et al[30] reported no significant difference in annular size or degree of aortic cusp calcification between patients with landing zone rupture and those with uncomplicated TAVR. Advanced MDCT analysis may provide useful parameters to predict the risk of landing zone complications, including (1) quantitative measurement of annular calcification (>550 Hounsfield units), (2) leaflet asymmetry, defined as:

$$\sqrt{[(\text{NC leaflet area} - \text{RC leaflet area})^2 + (\text{RC leaflet area} - \text{LC leaflet area})^2]}$$

and (3) annular cover index (calculated as prosthesis nominal area − annular area/prosthesis nominal area × 100). Notably, the multivariate MDCT-based risk model provides incremental predictive value compared with single anatomic features.

Condado et al[38] reported that focal calcification extending from the annular plane to at least 4 mm into the LVOT was present in 4 of 7 patients who experienced annular rupture. Similarly, Hayashida et al[39] suggested that significant calcification located in a particular vulnerable area, as revealed by MDCT, might be the possible mechanism for some cases of annular rupture. The vulnerable area was identified as the spot in the pericardial fat area of the annulus—an area uncovered by any cardiac structure and therefore at risk of mechanical stress at the time of forceful deployment of a balloon-expandable valve over a calcified nodule. Other authors reported the association between LVOT perforation and severe subannular calcification adjacent to the vulnerable muscular region of the LVOT (between the left fibrous trigone and the left/right aortic cusp commissure),[40] suggesting the critical importance of careful anatomic MDCT assessment and procedural planning.

The choice of valve prosthesis is also critical, and a self-expandable valve is preferable in cases with a high-risk LVOT calcification pattern and shallow sinuses of Valsalva (Figure 1).

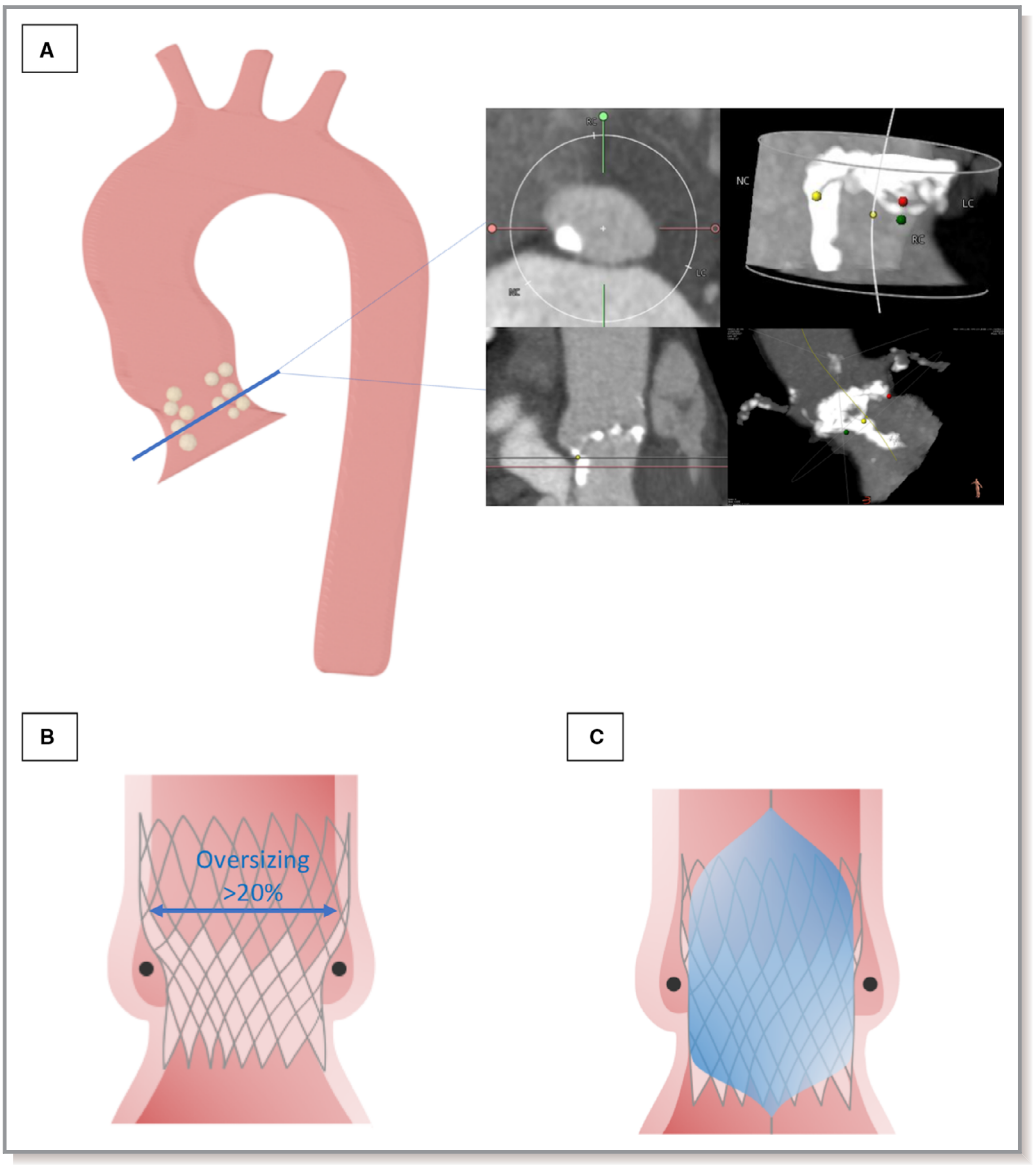


Figure 3. Procedural and anatomical risk factors for device landing zone rupture. Heavy calcification in the annular and left ventricular outflow tract region are important risk factors for device landing zone complications. Careful assessment of the baseline multidetector computed tomography provides important information on the presence of high-risk calcium distribution (**A**). Among the procedural variables, >20% area oversizing (**B**) and postdilatation (**C**) increase the risk of device landing zone rupture.

Additionally, it must always be noted when optimizing TAVR results that postdilatation significantly increases the risk of landing zone rupture, especially with >20% area oversizing (Figure 3).

How to Treat

In cases of uncontained rupture, conversion to emergency surgery is the only possible solution. Maintenance of hemodynamic stability is essential in the acute setting, and circulatory support should be immediately considered alongside a rapid search for the cause of hemodynamic instability using angiography and/or transthoracic/transesophageal echocardiography. In some cases, the correct diagnosis is established only by direct surgical exploration.[35]

Percutaneous coil embolization to seal the point of landing zone rupture has been described and may be a bailout option in cases of rapid deterioration.[41]

Contained rupture producing a periaortic hematoma has a less dramatic presentation. Pericardial drainage and/or observation may be initially considered in cases with limited injury and noncatastrophic clinical presentation. Nevertheless, close surveillance and repeated MDCT assessment remain important because adverse evolution is possible up to several hours or days from the rupture event.[35]

Device Embolization

Valve embolization is an infrequent yet important TAVR complication (Table 1) and accounts for ≈45% of emergency cardiac surgery in patients treated with TAVR.[42–47] Its occurrence imparts a 9-fold increase in mortality compared with uncomplicated cases.[31] Embolization usually happens acutely and intraprocedurally, though late device migration (up to 1 year after TAVR) has also been described.[48–50] Notably, the incidence of valve embolization has decreased over the years attributable to increasing institutional and operator experience and the availability of preplanning MDCT and newer-generation valves.[8,44,45,51]

Table 1. Incidence of Valve Embolization in TAVR

Study	Year(s)	Rate	References
Hamm et al	2011	0.5%	42
Gaede et al	2014–2016	0.2%	43
Ludman et al	2008–2015	0.2%–1.7%	44
Ludman et al	2016–2017	0.3%	45
Auffret et al	2010–2015	1.2%	46
Holmes et al	2012–2014	0.9%	47

TAVR indicates transcatheter aortic valve replacement.

Valve dislocations are either cranial toward the aorta or caudal into the LVOT/left ventricle. Aortic embolization is commonly the result of deployment in a high position and/or poor coaxial alignment of the device to the valve plane during implantation. Rarely, delivery system failure can lead to misalignment of the balloon and stent frame of balloon expandable systems or failed valve release in self- and mechanically expanding systems.[52]

Caudal migration toward the LVOT or left ventricle usually occurs because of low implantation depth, eccentric and asymmetric calcification, and more rarely because of device undersizing.[53]

How to Avoid

Avoidance of stored tension in the delivery system is important to prevent the risk of valve dislocation. During general anesthesia, a “breath hold” maneuver may be useful during valve deployment.

TAVR device migration can also arise during equipment retrieval after valve deployment. Inaccurate maneuvering of the pigtail catheter can hook the stent frame and snare the device during withdrawal. Use of a conventional 0.035-inch wire to straighten the pigtail facilitates safe removal.

How to Treat

Treatment options are strictly related to operator experience, clinical and anatomic factors, and the mechanics of device migration.

Hemodynamics determine initial management in the case of acute valve embolization. Where necessary, general anesthesia and femoral-femoral cardiopulmonary bypass can be considered before conventional cardiac surgery. Fortunately, hemodynamics are usually not catastrophic, and the dislocated valve can be snared and secured in a suitable position. Permanent fixation of the embolized valve may be achieved using an aortic stent (Figure 4), and a second valve can then be deployed in standard fashion. When caudal embolization occurs toward the LVOT/left ventricle, the choice is either to implant a second device to secure the embolized valve in a suitable subannular position or surgical removal of the embolized valve followed by transapical deployment of a second device or conventional surgical aortic valve replacement.[52–56]

If surgery is not an option because of prohibitive risk, the embolized valve can be dragged into a subannular position using a partially inflated valvuloplasty balloon under rapid ventricular pacing. Maintaining coaxial wire positioning is essential during this maneuver. A partially overlapping second valve can then be implanted to anchor the dislocated valve and prevent distal migration. Tiroch et al[55] described a successful case in which an Amplatz GooseNeck Snare (ev3; Endovascular Inc, Plymouth, MN) was used to retrieve a

Sapien 3 valve from the left ventricle after unsuccessful attempts using standard valvuloplasty balloons.

Coronary Occlusion

Coronary artery obstruction by leaflet material during TAVR is a relatively infrequent complication but has potentially catastrophic clinical consequences, with an associated mortality of up to 50%. Coronary occlusion occurs in <1% of native valve interventions and tends to involve the left main stem more frequently than the right coronary artery.[4]

Occlusion is typically caused by displacement of the calcified leaflets of the native aortic valve toward the coronary ostia valve implantation. Coronary flow obstruction can thus be related either to coverage of the coronary ostia or sealing of the sinus of Valsalva at the sinotubular junction. Identification of patients at high risk of coronary occlusion is therefore a key component of procedural planning. Anatomic features that predispose to coronary occlusion are low coronary height (<12 mm) and narrow sinus of Valsalva diameter (<30 mm).[57]

Intraprocedural coronary occlusion is more common during valve-in-valve procedures (TAVR within a failed surgical bioprosthesis) as a consequence of reduced distance between the valve leaflets and coronary ostia (attributable to the supra-annular design of surgical prostheses) and the narrower sinus of Valsalva (attributable to surgical bioprosthesis suturing). In particular, bioprosthetic valves with leaflets mounting outside an internal stent (eg, Mitraflow Sorin and Triflecta, St. Jude Medical Inc., St Paul, MN) or stentless bioprosthetic valves are at higher risk because the leaflets of these bioprostheses may extent outward beyond the surgical device implantation after TAVR.[58]

Coronary occlusion causes rapidly worsening severe hypotension with dynamic ST-segment changes in 50% and ventricular arrhythmias in 25% of cases.[57] Immediate angiographic assessment of coronary patency is required in patients in whom coronary occlusion is suspected.

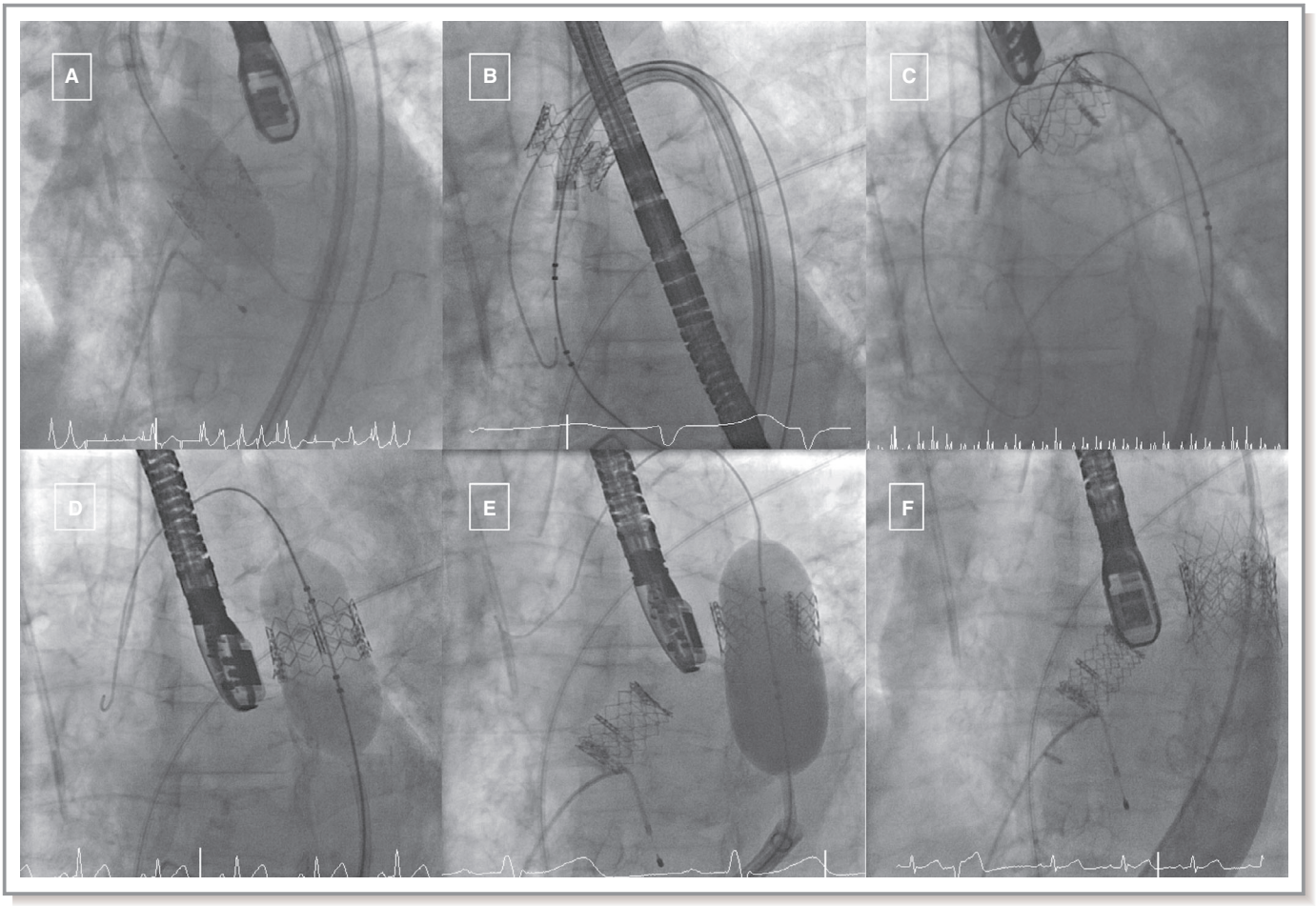


Figure 4. A case of aortic TAVR device embolization. In this case, a balloon-expandable Sapien XT valve was deployed in a standard fashion under rapid pacing (**A**). However, the device was dislocated into the aortic root during delivery system retrieval (**B**). The Sapien XT was snared and secured in a suitable position in the descending aorta (**C** and **D**). A second Sapien XT was deployed in the standard position (**E**) and an aortic stent used to secure the embolized valve position (**F**).

How to Avoid

Preprocedural cardiac MDCT is critical to identify patients at risk of coronary occlusion by measurement of the height of the coronary ostia in relation to the aortic annulus, the width and height of the sinus of Valsalva, and the width of the sinotubular junction.

In patients who are deemed at high risk, coronary protection with a standard 0.014-inch guidewire is advisable to help prevent and treat potential occlusion. In some cases, a preemptive coronary balloon or stent can be mounted on a guidewire and advanced in the left anterior descending artery and/or right coronary artery during valve deployment. If coronary occlusion occurs, the stent can be pulled back and deployed in a "chimney" fashion to maintain coronary patency[59] (Figure 5).

Although there are no prospective data, a repositionable TAVR valve is preferred in patients at high risk of coronary occlusion.

How to Manage

In patients in whom coronary occlusion occurs without a protective guidewire in situ, immediate cannulation of the affected coronary artery with a guiding catheter is required to allow balloon angioplasty. Coronary stent deployment with high-pressure postdilatation is often needed to avoid ostial deformation.

Engaging the coronary ostia with a TAVR device in situ may be difficult and requires dedicated strategies. Balloon-expandable valves are deployed in the subcoronary position and interact with the coronary arteries in <10% of cases—even then, coronary access through the valve struts is generally straightforward.[60] However, sudden coronary occlusion is more frequently observed with balloon expandable valves, especially following high implantation in an aortic root with shallow sinuses and low coronary ostia. The CoreValve Evolut self-expandable valve (Medtronic, Minneapolis, MN) is deployed in the supra-annular position, and coronary access can be difficult through the alternating diamond-shaped valve cells. Conversely, the ACURATE neo valve (Boston Scientific, Natick, MA), despite its self-expanding surpra-annular design, allows easy access to the coronary ostia thanks to the high commissure posts and a low sealing skirt profile. Moreover, the ACURATE neo is designed to minimally protrude into the LVOT, minimizing the risk of coronary occlusion.

The catheter of choice for the left coronary artery should be the Judkins left catheter with preference for a smaller size (3.5 instead of 4.0), or the Extra-Back-up catheter 3.5, maintaining the diagnostic 0.035-inch J-wire within the catheter to facilitate orientation of the catheter tip to engage the coronary ostia through the valve struts. The basic technique is to curl the J-wire against the valve leaflet and slide the catheter over to open the primary curve. At this point, the tip of the catheter usually passes through the valve strut to engage the left main ostium. Further catheter manipulation may be required to obtain the best coaxial engagement. The Judkins right catheter is effective for the right coronary artery in most cases.[60]

Coronary occlusion after self-expandable device deployment can be resolved by snaring the TAVR valve frame and lifting the deployed valve above the sinotubular junction. This option is not available after deployment of a balloon-expandable valve.

Recently, the BASILICA (Bioprosthetic or Native Aortic Scallop Intentional Laceration to Prevent Iatrogenic Coronary Artery Obstruction) trial assessed the safety and feasibility of transcatheter electrosurgery to lacerate the native aortic valve leaflets in patients with a high risk of coronary occlusion.[61] This is a modification of the LAMPOON procedure in which an electrified guidewire (Astato XS 20, Asahi Intecc USA, Santa Ana, CA) is used to lacerate the anterior mitral leaflet to prevent LVOT obstruction in patients undergoing transcatheter mitral valve replacement.[62] In the first experience on 30 high-risk patients, the procedure was successful in 95%, and there was 100% freedom from coronary occlusion during TAVR. This new transcatheter technique may thus prove useful in elective high-risk patients and as a bailout option for coronary occlusion. However, the safety of the procedure needs to be confirmed in larger studies because adverse cardiovascular events were observed in 30% of the cases, including 1 (3%) disabling stroke and 2 (7%) nondisabling strokes.[61]

Stroke

Recent trials in low-risk patients have demonstrated a low incidence of disabling stroke (0.6% and 0.5% at 30 days in the PARTNER 3 [Safety and Effectiveness of the SAPIEN 3 Transcatheter Heart Valve in Low-Risk Patients With Aortic Stenosis] and Evolut Low Risk trials, respectively) and noninferiority of TAVR compared with surgery with respect to stroke-free survival (HR, 0.25; 95% CI; 0.07–0.88; P=0.02 in PARTNER 3).[1,2] Nevertheless, stroke remains one of the most feared complications of TAVR, with a high risk of 30-day mortality (odds ratio [OR], 6.45; 95% CI, 3.9–10.6).[1,2,63] Contemporary data including different TAVR technologies in high- and intermediate-risk patients show a 30-day stroke rate ranging from 1.4% to 1.9%.[64–67] Subclinical new cerebral ischemic lesions are much more common and can be identified using diffusion-weighted magnetic resonance imaging in up to 80% of patients undergoing TAVR.[68]

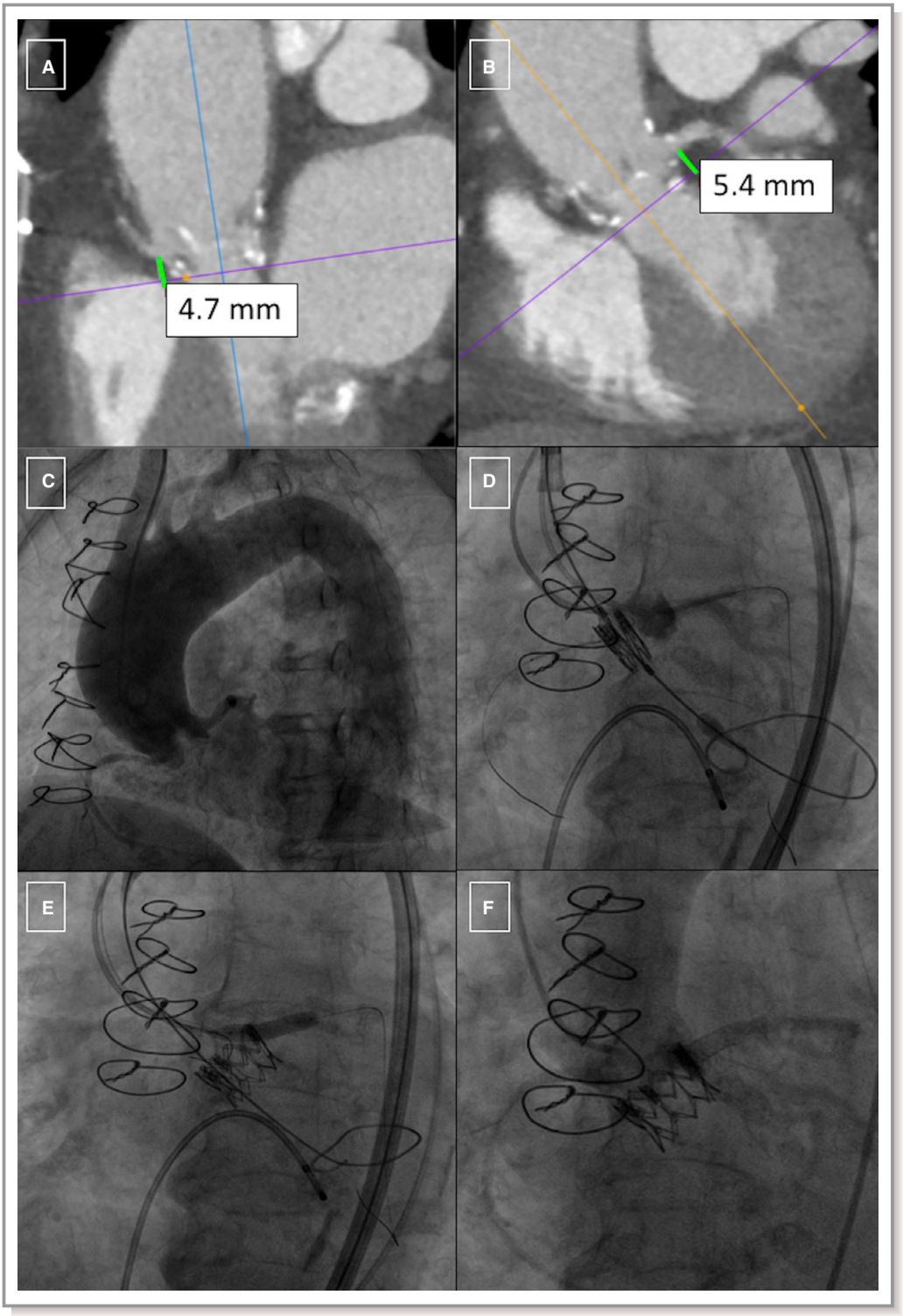
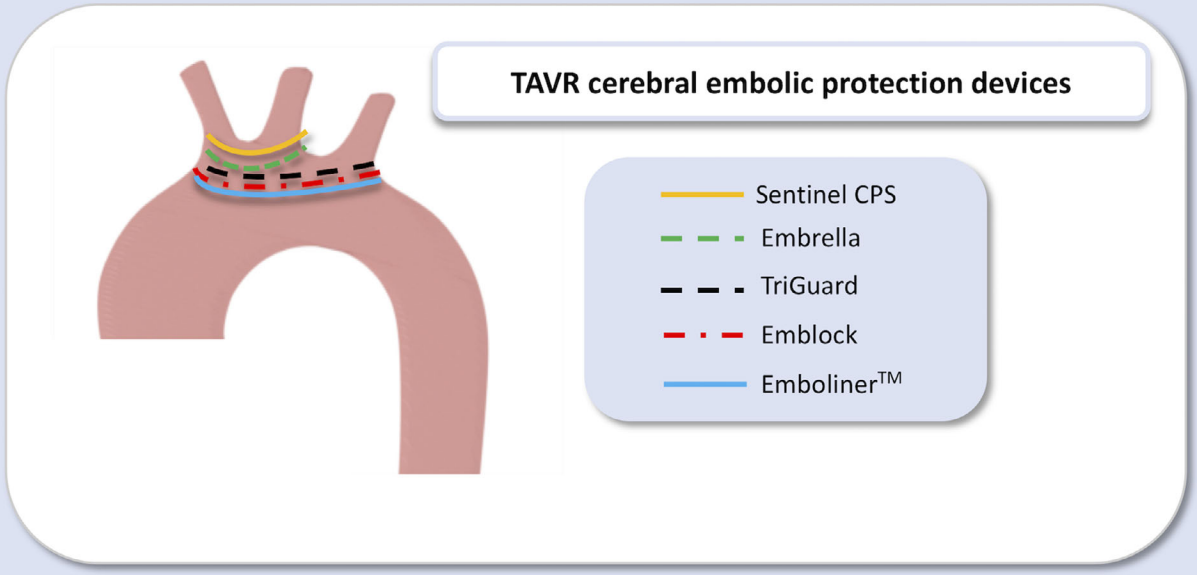


Figure 5. Preventive strategies to avoid coronary occlusion in a high risk valve-in-valve procedure. This case shows the wire and jailed stent protection technique in a patient with a degenerated Sorin Freedom stentless 23 mm valve (**A** through **C**). Baseline multidetector computed tomography and angiography showed the low bilateral coronary takeoff. An undeployed stent was prophylactically positioned in the left main stem (LMS) before advancing a Sapien XT 20-mm valve (**C** and **D**). Immediately after valve deployment, the patient's hemodynamics crashed and the coronary stent was inflated at high pressure in the LMS at the ostial position (**E**). The final aortogram showed the Sapien-XT valve in correct position and widely patent coronary arteries (**F**). Reprinted from Maggio et al[59] with permission. Copyright ©2017, Oxford University Press.



CEPD	Manufacturer	Sheath size	Arterial access	Technology
Sentinel CPS	Claret Medical Inc (Santa Rosa, California, USA)/Boston Scientific	6 French	Right radial/brachial	Proximal filter is deployed into the brachiocephalic, distal filter is deployed into the left common carotid artery
Embrella	Edwards Lifesciences (Irvince, California, USA)	6 French	Right radial/brachial	Umbrella-like filter (100μm) consisting in 2 polyurethane membranes mounted on a nitinol frame positioned across innominate and left carotid arteries.
TriGuard	Keystone Heart Ltd (Herzliya, Israel)	9 French	Femoral	Mesh filter (130μm)positioned across all supraortic vessel. Stabilizers in the innominate artery and inner curvature of the aortic arch.
Emblock	Innovative Cardiovascular Solutions	12 French	Femoral	Expandable filter (125μm) placed across the aortic arch, integrated in a 4F pig-tail catheter.
Emboliner™	Cardiological Solutions	9 French	Femoral	Circumferential design, positioned across the aortic arch. Expandable access port allows the passage of the TAVR device through the filter

Figure 6. Cerebral embolic protection device. The upper panel shows the degree of cerebral protection provided by currently available embolic protection devices. Devices that cover the brachiocephalic trunk and left common carotid arteries protect only 9 of 28 brain regions, considering the dual blood supply of the posterior cerebral circulation. TAVR indicates transcatheter aortic valve replacement.

The occurrence of TAVR-related stroke demonstrates a bimodal pattern of distribution, with up to 50% of events occurring within the first 24 hours after TAVR (dependent on clinical and procedural factors) and a late phase >10 days after TAVR (dependent on clinical characteristics—specifically, the atherosclerotic and overall frailty profile).[69] Among

early (0–10 days) patient-related predictors, those associated with stroke in multivariate models in the CoreValve trials were peripheral vascular disease (HR, 1.44; 95% CI, 1.03–2.00), prior transient ischemic attack (HR, 2.48; 95% CI, 1.67–3.67), angina (HR, 1.63; 95% CI, 1.15–2.33), body mass index <21 kg/m^2 (HR, 2.14; 95% CI, 1.37–3.34) and a previous fall (HR, 1.72; 95% CI, 1.20–2.47), while the absence of previous coronary artery bypass grafts was protective (HR, 0.58; 95% CI, 0.39–0.86). Among the procedural variables, total time in the catheterization laboratory (HR, 1.003; 95% CI, 1.000–1.005), total time of delivery system in the body (HR, 1.01; 95% CI, 1.004–1.02), and rapid pacing during valvuloplasty (HR, 9.86; 95% CI, 1.37–70.7) were associated with early stroke.[70]

Histopathology of debris collected by cerebral embolic protection devices (CEPDs) used during TAVR demonstrates that embolized tissue particles can originate from the aortic valve, the aorta, and the left ventricle and often involve a thrombus. The embolized material can cause cerebral ischemia itself or can trigger further thrombus development, thus explaining why the clinical manifestation (and consequent diagnosis) of early TAVR-related stroke can be delayed for up to 10 days.

How to Avoid

Optimal anticoagulation throughout the procedure is essential to minimize thrombus formation. The BRAVO (Effect of Bivalirudin on Aortic Valve Intervention Outcome) trial has shown that bivalirudin and heparin yield similar rates of major bleeding and ischemic cardiovascular events 30 days after TAVR.[71] Unfractionated heparin therefore remains the standard during TAVR, with a parenteral bolus followed by additional doses until an activated clotting time of 250 to 300 seconds is achieved.

CEPDs positioned across the origins of the supra-aortic vessels capture or deflect embolic debris away from the cerebral vasculature and potentially reduce the burden of ischemic strokes during TAVR. However, their use in current clinical practice remains limited, with <2% of CEPD-assisted TAVR in the Evolut Low Risk trial and even less in routine clinical practice.[2]

Use of CEPD has been associated with a smaller volume of silent ischemic lesions, although a recent meta-analysis failed to demonstrate a reduction in the number of single or multiple ischemic lesions.[72,73] Despite a significant reduction in 30-day stroke rate (OR, 0.55; 95% CI, 0.31–0.98), CEPDs have no impact on 30-day mortality (OR, 0.43; 95% CI, 0.18–1.05).[72]

A significant number of thromboembolic cerebral insults relate to territories supplied by the vertebral arteries (a segment of the cerebral circulation unprotected by most currently available CEPDs; Figure 6) and extended coverage across all the supra-aortic vessels (including the left subclavian artery) is preferable. However, most currently available devices (including the Sentinel CPS [Claret Medical Inc, Santa Rosa, CA] and Embrella [Edwards Lifesciences, Irvine, CA]) protect only the brachiocephalic and left common carotid arteries, which supply only 9 of 28 brain regions as a consequence of the dual posterior circulation blood supply.

The TriGuard device (Keystone Heart Ltd., Herzliya, Israel) is the only commercially available CEPD that allows complete coverage of the supra-aortic vessels. In the DEFLECT III (Prospective, Randomized Evaluation of the TriGuard HDH Embolic Deflection Device During Transcatheter Aortic Valve Implantation) trial, this device was successfully positioned in 89% of cases and appeared to mitigate new neurological deficits and cognitive impairment after transcatheter aortic valve implantation yielding a numeric greater freedom from new cerebral ischemic lesions (26.9% versus 11.5%) and smaller lesion volume (19.6 mm^3 versus 34.8 mm^3; P=0.07) and improved cognitive function compared with the control arm (P=0.028).[74]

Several new CEPDs that provide full coverage of the aortic arch are under evaluation for clinical use,[75] including the Emblock Embolic Protection System (Innovative Cardiovascular Solutions, LLC, Grand Rapids, MI) and the Emboliner Embolic Protection Catheter (Emboline Inc, Santa Cruz, CA). The Emblock device incorporates a 4F pigtail catheter to facilitate TAVR device positioning, while the Emboliner captures both cerebral and noncerebral emboli to provide full-body embolic protection.

The optimal combination (single versus double) and duration of antiplatelet therapy to mitigate the risk of thrombosis after TAVR has not been established,[76] and dual antiplatelet therapy (aspirin and clopidogrel) for 3 to 6 months is the most commonly used regime.

How to Manage

Diagnosis of periprocedural stroke is often delayed because patients are often under general anesthesia or conscious sedation. When stroke is considered, prompt access to computed tomography of the brain, computed tomography cerebral angiography, and specialist care by a dedicated stroke team are essential. Anectodal experiences suggest that mechanical thrombectomy may have a role in acute and late-presenting stroke following TAVR.[77]

Periprocedural Conduction Abnormalities

Conduction abnormalities requiring permanent pacemaker (PPM) implantation and development of new left bundle branch block (LBBB) remain the most common TAVR

complications.[78] Many patients with aortic stenosis have some conduction disease already, but the close proximity of the atrioventricular conduction system to the aortic valve apparatus makes it especially susceptible to injury during TAVR.[79]

Perioperative conduction abnormalities result from mechanical compression of the conduction tissue as a result of pre- or postdilatation, deep implant depth, or the use of self-expanding devices and those with longer stent frames.[80]

High-Grade Atrioventricular Block and PPM

The development of high grade atrioventricular block usually occurs within 24 hours of the procedure independent of the valve used.[81] However, 2% to 7% of patients can develop high-grade atrioventricular block beyond 48 hours and 85% to 90% of PPM implants are required within 7 days of the procedure (median 3 days).[81,82] Late-onset high-degree atrioventricular block is uncommon, and in one recent study no patients with a normal ECG 2 days after TAVR developed delayed high-degree atrioventricular block.[81] Similarly, 99.6% of patients without LBBB remained PPM free after 1 year.[83]

New LBBB

New-onset LBBB after SAVR is a predictor of syncope, atrioventricular block, and sudden cardiac death.[80]

After TAVR, the incidence of new periprocedural LBBB varies widely and is higher with self-expanding (18%–65%, Medtronic CoreValve) compared with balloon-expandable valves (4%–30%, Edwards Sapien/Sapien XT).[79,84] Studies of LBBB with new-generation valves are limited: 12% to 22% for Sapien 3 valve,[85,86] 34% for Evolut R,[87] and 55% to 77% for Boston Lotus valve.[1,2,88,89]

In PARTNER 3, the incidence of new LBBB at 1 year was 23.7% in the TAVR cohort compared with 8.0% in the SAVR cohort (HR, 3.43; 95% CI, 2.32–5.08).[1] LBBB usually develops within 24 hours of TAVR (85%–94%) and may resolve within 30 days, but 55% of patients have persistent LBBB.[78] The main predictors are use of a self-expandable valve (OR, 2.5–8.5),[90–92] depth of prosthesis within the LVOT (OR, 1.15–1.4/1 mm),[93–95] overexpansion of the native aortic annulus (OR, 5.3 if >15%),[93,96] and larger valve size.[83,84]

There are limited studies evaluating the association of new LBBB and need for PPM implantation, but 2 recent meta-analyses[97,98] suggested a 2-fold higher risk of PPM implant in patients with new LBBB after TAVR. Approximately 8% to 19% of patients with new LBBB require a PPM, the most frequent indication being progression to atrioventricular nodal block.[83,99–101] New LBBB is also associated with higher cardiovascular mortality (OR, 1.39; CI, 1.04–1.86),[97] especially in patients with QRS >160 ms (HR, 4.78; CI, 1.56–14.53).[102]

How to Prevent

Conduction disturbances in patients undergoing TAVR are largely dependent on unmodifiable patient-related risk factors, including electrical and anatomic variables. Baseline right bundle branch block is the strongest and most consistent risk factor for PPM regardless of valve type (OR, 2.8–46.7).[78,79,96] First-degree atrioventricular block is also strongly associated (OR, 4.0–11.4).[103–105] Among anatomic predictors, the presence of calcification below the aortic annulus and in the LVOT increases the risk for PPM (OR, 1.03–4.7).[103,106]

Procedural variables are also important. In a recent systematic review,[107] the rate of PPM varied considerably depending on the type of valve deployed—self- and mechanically expanding valves (CoreValve/Evolut/Lotus) have a consistently higher risk of PPM[107] (Medtronic CoreValve versus Edwards Sapien/Sapien XT; OR, 2.6–25.7)[79] (Table 2). In PARTNER 3 (using the Sapien 3 valve) there was no difference in PPM rate between TAVR and surgery (6.6% versus 4.1%; HR, 1.65; 95% CI, 0.92–2.95), while the Evolut Low Risk study showed a higher rate of PPM in the TAVR group (17.4% versus 6.1%).

Depth of implantation is also strongly associated with increased risk of PPM regardless of the type of prosthesis (OR, 1.1–1.5/1 mm of LVOT).[84,89,106,108–110] (Table 3). Another factor is oversizing/stretching of aortic annulus by 10% to 15%, which increases the risk of PPM with first-generation devices.[84]

The baseline risk of developing conduction abnormalities may also influence the strategy of pacing support during the TAVR procedure. Rapid ventricular pacing is indeed often required during balloon aortic valvuloplasty or valve deployment and use of pacing via the left ventricular guidewire is an established technique to simplify the procedure and reduce the risk of vascular complications and pericardial effusion.[111]

Table 2. Rate of Permanent Pacemaker Implantation

Valve	Permanent Pacemaker Implantation Rate (%)
Sapien/Sapien XT	2.3–28.2
Sapien 3	4–24
CoreValve	16.3–37.7
Evolut R	14.7–26.7
Lotus	27.9–36.1
Direct flow medical	17
Portico	13.5
JenaValve	14.4
Accurate Neo	2.3–10.2

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Table 3. Risk of Conduction Disturbances According to the Depth of Implantation

Valve Prosthesis	Proposed Cutoff Values	References
Edwards Sapien XT	6.3 mm	108
Edwards Sapien 3	7 mm or 25% of stent frame	106, 108
Medtronic CoreValve	6–7.8 mm	109, 110
Lotus	5–6.7 mm	89, 108

However, left ventricular guidewire pacing could expose the patient to a period of hemodynamic instability if the left ventricular guidewire was removed prematurely. Thus, a right ventricular temporary pacing wire may be preferable in patients at high risk of periprocedural conduction disturbances. Prophylactic PPM implantation may also be considered in patients with preexisting high-grade conduction abnormalities (Figure 1).

How to Manage

The prognostic implications of PPM after TAVR are currently unclear, with conflicting data. Registry data from the United States[99] showed increased mortality in patients requiring PPM (HR, 1.31; CI, 1.09–1.58), whereas other studies observed mortality reduction (HR, 0.31; CI, 0.11–0.85).[108] Furthermore, a recent systematic review[107] and meta-analysis[112] have shown no association between PPM and all-cause mortality.

The European Society of Cardiology guidelines[113] suggest 7 days of observation for stable high-degree atrioventricular block before PPM implant, in contrast with current routine clinical practice, where 50% of patients receive a PPM within 3 days of TAVR.[97] Recovery of intrinsic rhythm has been observed in up to 50% of paced patients at the time of TAVR follow-up.[114,115]

Clear indications are crucial, as PPM implantation exposes patients to prolonged hospital stay, risk of infection, thromboembolism, and suboptimal functional recovery. While immediate PPM implant can be considered in stable patients with preexisting conduction disease (right bundle branch block and first-degree atrioventricular block) who develop high-grade atrioventricular block during valve deployment, spontaneous recovery of atrioventricular node function might occur within 24 hours of observation in cases without preexisting conduction disorder.

Management of new LBBB following TAVR remains controversial. The general consensus is for a period (48–72 hours) of inpatient monitoring to detect possible progression to atrioventricular nodal block and need for PPM implant. Persistent LBBB with QRS >160 ms and associated first-degree heart block may require prophylactic PPM. An implantable loop recorder may be an option when LBBB persists and further studies are required to define optimal management.

General Considerations and Conclusion

The PARTNER 3 trial has shown superiority of TAVR for the composite end point of mortality, stroke, and hospital readmission at 1 year (HR, 0.38; 95% CI, 0.15–1.00) compared with SAVR. Similarly, the Evolut Low Risk trial demonstrated the noninferiority of TAVR versus SAVR regarding the composite primary end point of death and stroke (5.3% versus 6.7%) with a longer follow-up of 2 years.[1,2] If confirmed at long-term follow up, these favorable results in low-risk patients will drive expanded indications for TAVR. Focus on the prevention and treatment of procedural complications is therefore essential.

Before any TAVR procedure, it is essential for the heart team to discuss bailout options, including whether conversion to open heart surgery is appropriate. Procedural planning is key to prevent potentially catastrophic complications, including landing zone rupture, device embolization, or coronary occlusion. Preprocedural imaging is essential to plan vascular access, and intravascular lithotripsy may have a role in high-risk cases. Further studies are warranted to define the place of CEPDs in reducing the risk of stroke during TAVR and the indications for their use. Ultimately, all members of the heart team need to understand strategies for the prevention and management of procedural complications during TAVR. This will produce a more predictable procedure with better long-term outcomes for more of our patients with aortic stenosis.

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Key Words: annular rupture • aortic stenosis • cardiovascular complications • pacemaker • stroke • transcatheter aortic valve implantation • transfemoral aortic valve implantation

SUPPLEMENTAL MATERIAL

Table S1. VARC2 vascular access site and access-related complication.

Major vascular complication
Any aortic dissection, aortic rupture, annulus rupture, left ventricle perforation, or new apical aneurysm/pseudo-aneurysm OR
Access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudoaneurysm, haematoma, irreversible nerve injury, compartment syndrome, percutaneous closure device failure) *leading to* death, life-threatening or major bleeding, visceral ischemia or neurological impairment OR
Distal embolization (non-cerebral) from a vascular source requiring surgery or resulting in amputation or irreversible end-organ damage OR
The use of unplanned endovascular or surgical intervention associated with death, major bleeding, visceral ischemia or neurological impairment OR
Any new ipsilateral lower extremity ischaemia documented by patient symptoms, physical exam, and/or decreased or absent blood flow on lower extremity angiogram OR
Surgery for access site-related nerve injury OR
Permanent access site-related nerve injury
Minor vascular complications
Access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudoaneurysm, haematoma, irreversible nerve injury, compartment syndrome, percutaneous closure device failure) *not leading to* death, life-threatening or major bleeding, visceral ischemia or neurological impairment OR
Distal embolization treated with embolectomy and/or thrombectomy and not resulting in amputation or irreversible end-organ damage OR
Any unplanned endovascular stenting or unplanned surgical intervention not meeting the criteria for a major vascular complication OR
Vascular repair or the need for vascular repair (via surgery, ultrasound-guided compression, transcatheter embolization, or stent graft) OR
Percutaneous closure device failure
Failure of a closure device to achieve haemostasis at the arteriotomy site leading to alternative treatment (other than manual compression or adjunctive endovascular ballooning).

Supplemental Reference:

1. Kappetein AP, Head SJ, Généreux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, van Es G-A, Hahn RT, Kirtane AJ, Krucoff MW, Kodali S, Mack MJ, Mehran R, Rodés-Cabau J, Vranckx P, Webb JG, Windecker S, Serruys PW and Leon MB. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document (VARC-2)†. *Eur J Cardiothorac Surg*. 2012;42:S45-S60.