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Review Article

Stroke After Transcatheter Aortic Valve Replacement: Incidence, Definitions, Etiologies and Management Options

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Neurologic complications after transcatheter aortic valve replacement are devastating. The etiologies of stroke in this setting are best addressed in an integrated fashion during each phase of the perioperative pathway. The conduct of this triphasic approach will continue to be refined to reduce the stroke risks even further, given the major focus on aspects such as embolic protection devices and valve thrombosis. This neurologic focus in transcatheter aortic valve replacement has transformed the investigational approach to neurologic events in cardiovascular clinical trials, resulting in novel guidelines for the diagnosis and assessment of neurologic injury after cardiovascular interventions.

Key Words: transcatheter aortic valve replacement; stroke; transient ischemic attack; cognitive function; mortality; cerebral embolism; heparin; bivalirudin; platelet blockade; novel oral anticoagulants; modified Rankin scale; infarction; hemorrhage; diffusion weighted magnetic resonance imaging; transcranial Doppler; balloon-inflatable valve; self-expanding valve; embolic protection; aortic arch; Embrella device; Montage device; Sentinel device; Triguard device; thrombosis; definitions; trial endpoints; Valve Academic Research Consortium; Neurologic Academic Research Consortium; Society of Thoracic Surgeons; American Heart Association; American Stroke Association; American College of Cardiology

SINCE THE CLINICAL advent of transcatheter aortic valve replacement (TAVR) in 2002, this procedure has matured steadily to become a mainstream therapy for severe aortic stenosis.[1–3] As the continuing advances in TAVR permeate the clinical management of severe aortic stenosis across the world, the procedural volume likely will continue to grow, especially as the indications for TAVR migrate toward low-risk patients.[3,4] Landmark randomized clinical trials have demonstrated the safety and effectiveness of TAVR in excessive-risk and high-risk patients with aortic stenosis, resulting in commercial approval in the United States in 2011 and 2012, respectively.[5,6] In 2016, commercial approval for TAVR was extended to intermediate-risk patients after high-quality evidence demonstrated its outcome equivalence to surgical aortic valve replacement in the setting of severe aortic stenosis.[7]

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Table 1
Definitions of Stroke from the Valve Academic Research Consortium

Diagnostic features	Neurologic deficit confirmed by a neurologic specialist with at least 1 of the following: Change in level of consciousness Visual field deficit such as amaurosis fugax or hemianopia Motor deficit, such as hemiparesis or hemiplegia Speech and language deficit, such as dysarthria, dysphasia, or aphasia Other neurologic features consistent with stroke
Stroke	Duration of a focal or global neurologic deficit $\geq$ 24 h, new hemorrhage or infarct demonstrated using neuroimaging, or neurologic deficit resulting in mortality
Transient ischemic attack	Duration of a focal or global neurologic deficit $\leq$ 24 hours with no hemorrhage or infarct on neuroimaging if available and no alternative etiology for the neurologic presentation (eg, drugs, infection, hypoglycemia)
Types of stroke	Hemorrhagic: acute neurologic deficit due to intraparenchymal, intraventricular, or subarachnoid hemorrhage in the brain or spinal cord Ischemic: acute neurologic deficit due to infarction of the brain or spinal cord Undetermined: insufficient data to classify a stroke as hemorrhagic or ischemic
Stroke severity	Disabling stroke: a stroke with a score $\geq$ 2 at 90 days using the modified Rankin scale with an increase of at least 1 Rankin category from the pre-stroke clinical baseline Nondisabling stroke: a stroke with a score $\leq$ 2 at 90 days using the modified Rankin scale without an increase of at least 1 Rankin category from the pre-stroke clinical baseline (see Table 2 for the definition of the modified Rankin scale)

Adapted from Leon et al[15] and Kappetein et al.[16]

Current randomized trials are taking place to evaluate the outcome effects of TAVR in low-risk patients with aortic stenosis with both balloon-expandable and self-expanding devices.[1,8] The level of procedural risk in TAVR has been defined using the perioperative risk of mortality score developed by the Society of Thoracic Surgeons (STS) as follows: low-risk patients have an STS score $<$ 4%; intermediate-risk patients have an STS score between 4% to 8%; high-risk patients have an STS score $>$ 8%; and excessive-risk patients have an STS score typically beginning at $>$ 12%.[1–3,8,9]

Despite the impressive advances in TAVR in the last 15 years, clinical stroke has persisted as an important complication.[1,2,8,9] This narrative review focuses on this complication of TAVR with respect to its incidence, definition, etiologies, and neuroprotective strategies. This clinical update is important for the cardiac anesthesia community because interventional innovations likely will be integrated into the TAVR procedure to minimize the risk of stroke even further.

Incidence of Stroke After TAVR

The incidence of clinical stroke after TAVR currently is $<$ 5%. In an analysis examining the STS/American College of Cardiology Transcatheter Valve Therapy Registry from November 2011 to June 2013, the investigators reported a stroke rate of 4.1% at 1 year in a large cohort of 12,182 patients.[10] In a meta-analysis of 10,037 patients who underwent TAVR (2004-2011) in Europe and North America, the incidence of stroke was 1.5% $\pm$ 1.4% at 24 hours, 3.3% $\pm$ 1.8% at 30 days, and 5.2% $\pm$ 3.4% at 1 year.[11] Furthermore, in that analysis, the mortality risk at 30 days was 3.5-fold higher in the presence of a stroke (25.5% $\pm$ 21.9% *v* 6.9% $\pm$ 4.2%), highlighting the major outcome importance of stroke in TAVR and explaining the clinical priority given to this complication.[11]

In a meta-analysis (n = 16,063; 49 trials published by 2012), the incidence of stroke was 2.9% (95% confidence interval [CI] 2.4-3.4) at 30 days.[12] Stroke risk has decreased steadily since the earlier landmark clinical trials reported the stroke incidence to be in the 5% to 10% range, likely due to factors such as high patient risk and limited operator experience.[5,7,13] In an updated meta-analysis (n = 29,043), the incidence of stroke was 3.1%.[14] Furthermore, stroke independently predicted mortality after TAVR (odds ratio [OR] 6.45; 95% CI 3.90-10.66; p $<$ 0.0001).[14] In summary, the current evidence base reveals that stroke still is a common and important complication associated with TAVR, providing the justification for this focused narrative review.

Definition of Stroke After TAVR

The definition of stroke was addressed in a comprehensive fashion by the Valve Academic Research Consortium (VARC).[15,16] In this definition, a stroke was defined as neurologic deficit that persists longer than 24 hours with or without demonstrable new hemorrhage or infarction in the brain or spinal cord (Table 1).[16] Furthermore, the VARC definition of stroke also addresses the severity of stroke according to the modified Rankin scale, with a stroke categorized as disabling or nondisabling (Tables 1 and 2).[15–17]

Table 2
The Modified Rankin Scale for Classification of Stroke Severity

Level 0	No disability–no restriction of usual activities
Level 1	No significant disability–able to carry out all usual activities despite neurologic deficits
Level 2	Slight disability–able to look after own affairs without assistance but is unable to carry out all previous activities
Level 3	Moderate disability–requires some help but is able to walk without any assistance
Level 4	Moderately severe disability–cannot to attend to own bodily needs without assistance or requires assistance to walk
Level 5	Severe disability–requires constant nursing care and attention
Level 6	Death

Adapted from Sacco et al.[18]

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