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Influence of Transcatheter Aortic Valve Replacement Strategy and Valve Design on Stroke After Transcatheter Aortic Valve Replacement

A Meta-Analysis and Systematic Review of Literature

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Objectives The study undertook a systematic review to establish and compare the risk of stroke between the 2 widely used approaches (transfemoral [TF] vs. transapical [TA]) and valve designs (CoreValve, Medtronic, Minneapolis, Minnesota vs. Edwards Valve, Edwards Lifesciences, Irvine, California) for transcatheter aortic valve replacement (TAVR).

Background There has been a rapid adoption and expansion in the use of TAVR. The technique is however far from perfect and requires further refinement to alleviate safety concerns that include stroke.

Methods All studies reporting on the risk of stroke after TAVR were identified using an electronic search and pooled using established meta-analytical guidelines.

Results 25 multicenter registries and 33 single-center studies were included in the analysis. There was no difference in pooled 30-day stroke post-TAVR between the TF and TA approach in multicenter (2.8% [95% confidence interval (CI): 2.4 to 3.4] vs. 2.8% [95% CI: 2.0 to 3.9]) and single-center studies (3.8% [95% CI: 3.1 to 4.6] vs. 3.4% [95% CI: 2.5 to 4.5]). Similarly, there was no difference in pooled 30-day stroke post TAVR between the CoreValve and Edwards Valve in multicenter (2.4% [95% CI: 1.9 to 3.2] vs. 3.0% [95% CI: 2.4 to 3.7]) and single-center studies (3.8% [95% CI: 2.8 to 4.9] vs. 3.2% [95% CI: 2.4 to 4.3]). There was a decline in stroke risk with experience and technological advancement. There was no difference in the outcome of 30-day stroke between TAVR and surgical aortic valve replacement.

Conclusions Our findings suggest that the risk of 30-day stroke after TAVR is similar between the approaches and valve types. There has been a decline in stroke risk after TAVR with improvements in valve technology, patient selection, and operator experience. (J Am Coll Cardiol 2014;63:2101–10) © 2014 by the American College of Cardiology Foundation

Transcatheter aortic valve replacement (TAVR) has seen an exponential utilization in high surgical risk patients and an expansion to the intermediate risk population (1,2) due to impressive results in randomized PARTNER (Placement of AoRTic TraNscathetER Valve Trial) (Online Refs. e18,e19). Despite the growth, TAVR as a procedure is still evolving and requires further refinement to reduce complications. Stroke remains a major concern after TAVR and an important cause of increased morbidity and mortality. In the PARTNER trial cohort A and cohort B (Online Refs. e18,e19), the occurrence of stroke was doubled in the TAVR arm when compared to surgery (4.6% vs. 2.4%) and medical therapy (6.7% vs. 1.7%), respectively. Similarly, the risk of stroke in the TAVR arm of the PARTNER trials was also higher than that reported in the surgical literature for isolated aortic valve replacement (1.5% to 4%), raising safety concerns (3,4).

An understanding of the mechanisms underlying stroke after TAVR is therefore essential for the implementation of appropriate preventive measures prior to further expansion in its utilization. The manipulation of bulky endovascular devices along the aortic arch and aortic root during the transfemoral (TF) approach and manipulation

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Abbreviations and Acronyms

CI = confidence interval
MC = Medtronic CoreValve
OR = odds ratio
SAVR = surgical aortic valve replacement
TA = transapical
TAVR = transcatheter aortic valve replacement
TF = transfemoral
VARC = Valve Academic Research Consortium

of the apex during the transapical (TA) approach have been implicated for embolic strokes (5,6). Similarly, difference in valve design and deliverability between the self-expanding CoreValve, Medtronic, Minneapolis, Minnesota, and balloon expanding Edwards Valve, Edwards Lifesciences, Irvine, California have also been speculated to alter the stroke risk after TAVR (5) (Online Ref. e100). However, neither of these theories regarding valve delivery or valve type has been conclusively shown to alter risk of stroke after TAVR. Therefore, we undertook a comprehensive meta-analysis firstly, to establish and compare the risk of stroke between the 2 widely used valves (CoreValve vs. Edwards Valve) and approaches (TF vs. TA) for TAVR. Second, we looked at the temporal trend in stroke risk with experience and advancement in valve technology. Third, we compared the risk of stroke between TAVR and surgical aortic valve replacement (SAVR) in matched patient cohorts.

Methods

Study selection. We conducted this systematic review on published literature of stroke following TAVR using the QUOROM (Quality of Reporting of Meta Analysis) (7) and MOOSE (Meta Analysis of Observational Studies in Epidemiology) guidelines (8). A computerized search was performed to identify all relevant studies published until July 2013 in the PubMed database by 2 reviewers (G.A. and D.G.). The following search terms were used: *TAVI*, *Percutaneous Valves*, *Transcutaneous Aortic Valve*, and *Transcatheter Aortic Valve*. Citations were screened at the title and abstract level and retrieved as a full report if they reported on outcome of stroke after TAVR. Limiting the search parameters to the English language was applied subsequently. The full texts and bibliography of all potential articles were further reviewed in detail (G.A.) to seek additional relevant studies. Major conference proceedings were also searched to retrieve unpublished studies until November 2013.

Full text and references of all identified potential publications and conference proceedings were searched to select the reports for inclusion in the secondary analysis.

Inclusion criteria. Studies were included if the following criteria applied: 1) enrollment for TAVR was based on existing and accepted guidelines; 2) enrolled consecutive patients; 3) reported data on stroke following TAVR using a particular approach or valve design; and 4) performed a minimum of 75 successful TAVR procedures and at least 50 by a particular approach or valve type when from a single center. When 2 similar studies were reported from the same institution or author, the most recent publication or the publication with most information on stroke post TAVR was included in the analysis.

Exclusion criteria. Studies were excluded if any of the following criteria applied: 1) duplicate publication, overlap of patients, subgroup studies (nonconsecutive) of a main study; 2) lack of data on stroke by a particular approach or valve design; 3) if a valve other than the CoreValve or Edwards Valve was used; 4) if they were studies on valve in valve procedure; and 5) non-English reports.

Data extraction. Relevant information was collected by G.A./D.G. and included, but was not limited to, first author, year and journal of publication, study design, inclusion exclusion criteria, definition of stroke/transient ischemic attack, number of subjects included, subjects undergoing successful TAVR, type of device and approach used, study population demographics, follow up time period and primary and secondary outcomes.

Study endpoints. The primary end points evaluated were: 1) 30-day risk of stroke after TF and TA approaches; and 2) 30-day risk of stroke after CoreValve and Edwards Valve implantation. The results were stratified into single-center or multicenter experience. Secondary end points of interest were: 30-day risk of stroke after: 1) TAVR feasibility studies; 2) early TAVR experience vs. overall experience of large volume centers; and 3) TAVR vs. SAVR.

Definitions. 30-DAY STROKE. For the purpose of the current analysis, we used the following: 1) study-reported 30-day stroke when available; 2) in-hospital/procedural stroke when 30-day stroke was not available; and 3) combined major and minor stroke if reported separately.

The definition of stroke was as reported by the primary study.

FEASIBILITY STUDIES. Represent the initial studies prior to European Conformite Europeenne approval for the particular valve design.

HIGH-VOLUME CENTERS. Centers that had performed 100 or more TAVR procedure for a particular valve/approach.

EARLY EXPERIENCE OF HIGH-VOLUME CENTERS. The first 30% to 50% (or closest available) of patients enrolled by a center for a particular approach or valve design.

Statistical analysis. DerSimonian and Laird's (9) random effects model was utilized to pool the estimates of 30-day stroke from individual studies and subgroups. A random-effects model was also used to obtain a single pooled estimate of the odds ratios. The effect across subgroups was compared using a Q test based on analysis of variance. Statistical significance was set at a p value <0.05 (2-tailed). Heterogeneity, which was anticipated to be significant, was assessed by a Q statistic and I^2 test. Significant heterogeneity was considered present for p values <0.10 and/or an $I^2 = >50\%$. Sensitivity analysis was performed by excluding reports that did not use the Valve Academic Research Consortium proposed endpoints/definitions.