



Correspondance

Supra annular sizing for TAVR in bicuspid aortic valve stenosis: A meta-analysis

**Keywords:**

Transcatheter aortic valve replacement
 Bicuspid aortic valve
 Supra-annular sizing
 Permanent pacemaker implantation

Transcatheter aortic valve replacement (TAVR) has replaced surgical aortic valve replacement (SAVR) as a standard of care in aortic stenosis among high and intermediate surgical risk subjects. Recent studies have also reported the efficacy and safety of TAVR in low surgical risk patients. As annular ring represents the narrowest part of the aortic root in a tricuspid aortic valve, multidimensional computed tomography with annular sizing is conventionally used to determine the size of the valve. With the prevalence of bicuspid aortic valve (BAV) being around 1–2% and its complex aortic root morphology, the role of supra annular sizing has been suggested by various authors. Also, most large randomised control trials studying TAVR in aortic stenosis exclude BAV, and hence, the procedural techniques and clinical outcomes cannot be generalized. In a propensity score matched retrospective study, TAVR in BAV was associated with no difference in survival, whereas it was associated with higher incidence of stroke, annulus rupture and need for permanent pacemaker implantation (PPI).¹ While increased incidence of stroke can be attributed to embolic ethology from the calcified BAV, increased incidence of annulus rupture and need for permanent pacemaker implantation can be accredited to potential oversizing of bio-prosthetic valves in BAV. Hence, an updated meta-analysis of studies reporting the annular and supra annular diameter in patients with BAV, with clinical outcomes following supra-annular sizing in TAVR was conducted.

A comprehensive electronic search across PubMed/Medline and Cochrane database for relevant articles was conducted using the keywords “Bicuspid aortic valve”, BAV, “Supra-annular sizing”, “Transcatheter aortic valve replacement”, TAVR, TAVI, “Transcatheter aortic valve implantation”. The database search was augmented with a bibliographic search of relevant articles. A study was included if it reported annular and supra-annular measurements of the aortic root in a patient with BAV. Title and abstracts were screened by two individual authors followed by data extraction. Data affiliated to event rates among patients treated with TAVR in compliance with supra-annular sizing was also extracted. Since individual studies had ethical review board approval, no additional ethical clearance was deemed necessary for this meta-

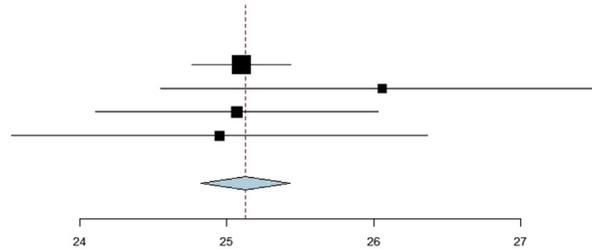
analysis. We used inverse variance method with fixed effect model to pool mean annular and supra-annular diameter. Heterogeneity was measured using the I^2 value, and defined as $I^2 > 50\%$. In studies reporting median and inter quartile range instead of mean and standard deviation, we used the method provided by Luo et al. and Wan et al. to calculate the same.^{2,3} The perimeter derived diameter was used for pooled estimate whenever possible. We used 0.5 as the correction factor for studies with zero event rates. All analyses were carried out using R (R Core Team (2013). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <http://www.R-project.org/>.)

Database search revealed a total of four articles, of which three were included. One study was included following manual search. Finally, four studies which included a total of 240 BAV were analysed. Two studies used mechanically expanding valves, one study used self-expanding valves and one study a combination of self-expanding and balloon expanding valves. The pooled mean annular diameter was 25.12 mm [95% confidence interval 24.82–25.43] (Fig. 1, Panel A), whereas the pooled mean supra-annular diameter was 24.12 mm [95% confidence interval 23.8–24.43] (Fig. 1, Panel B). Mortality was not reported in any trial (two offour included trials which reported clinical outcomes) among patients treated with TAVR with supra-annular sizing. The pooled incidence of stroke among patients treated with TAVR with supra-annular sizing was 0.069 [95% confidence interval –0.039–0.117] (Fig. 2, Panel A). The pooled incidence of permanent pacemaker implantation among patients treated with TAVR with supra-annular sizing was 0.097 [95% confidence interval –0.088–0.280] (Fig. 2, Panel B). There was no heterogeneity associated with any of the pooled estimates.

To the best of our knowledge this is the first meta-analysis studying supra annular sizing for TAVR in BAV. Though, our meta-analysis reported a statistically significant difference in annular and supra-annular diameter, the difference was not of any clinical significance with respect to choice of TAVR size.⁴ Our result was consistent with the study from the BAVARD multicentre registry which concluded that annular sizing in BAV is appropriate with minimal oversizing.⁵ Determining optimal sizing is crucial for improved clinical outcomes following the procedure, mostly related to para-valvular leak, risk of embolism, rate of permanent pacemaker implantation and to increase the overall performance of the prosthetic valve. Several studies have reported overstretching with a prosthetic valve as one of the important cause of conduction block resulting in PPI. Moreover, studies have reported increased in-hospital mortality, and length of hospital stay in patient's undergoing PPI following TAVR. The incidence of PPI has

PANEL A : Pooled mean annular diameter

Studies	Estimate (95% C.I.)
Kim WK et al. 2019	25.100 (24.763, 25.437)
Jegar R et al. 2018	26.060 (24.549, 27.571)
Liu X et al. 2018	25.070 (24.108, 26.032)
Xiong T Y et al. 2018	24.950 (23.536, 26.364)
Overall (I²=0 % , P=0.668)	25.129 (24.825, 25.433)



PANEL B : Pooled mean supra-annular diameter

Studies	Estimate (95% C.I.)
Kim WK et al. 2019	25.000 (24.613, 25.387)
Jeger R et al. 2018	23.490 (22.118, 24.862)
Liu X et al. 2018	22.130 (21.440, 22.820)
Xiong T Y 2018	22.260 (21.090, 23.430)
Overall (I²=0 % , P< 0.001)	24.120 (23.804, 24.436)

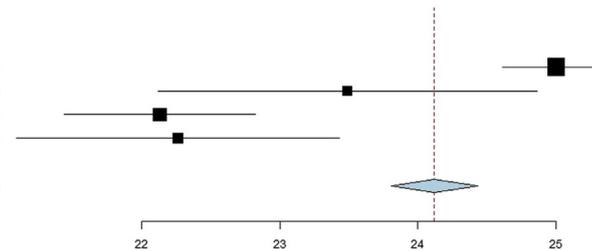
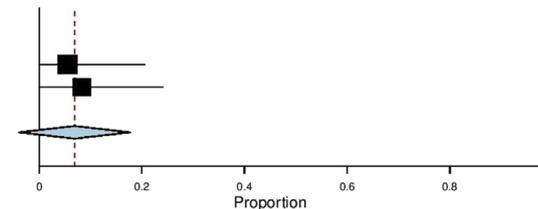


Fig. 1. PANEL A - Forest plot for pooled mean annular diameter using inverse variance method with fixed effect model. **PANEL B**- forest plot for pooled man supra-annular diameter using inverse variance method with fixed effect model. All measures in millimeter (mm).

PANEL A : Stroke

Studies	Estimate (95% C.I.)	Ev/Trt
Jeger et al. 2018	0.056 (0.000, 0.205)	0/8
Liu et al. 2018	0.083 (0.000, 0.240)	1/12
Overall (I²=0 % , P=0.801)	0.069 (-0.039, 0.177)	1/20



PANEL B : Permanent pacemaker implantation

Studies	Estimate (95% C.I.)	Ev/Trt
Jeger et al. 2018	0.250 (0.000, 0.550)	2/8
Liu et al. 2018	0.038 (0.000, 0.143)	0/12
Overall (I²=41.27 % , P=0.192)	0.096 (-0.088, 0.280)	2/20

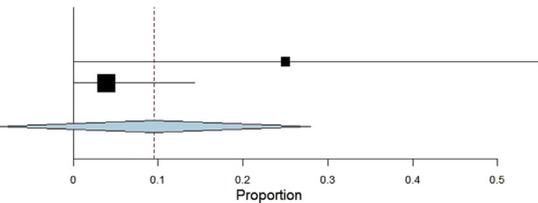


Fig. 2. PANEL A - Pooled incidence of stroke following supra-annular sizing of TAVR in BAV. **PANEL B**- Pooled incidence of permanent pacemaker implantation following supra-annular sizing of TAVR in BAV. Der-Simonian and Laird method was used to pool event rates.

varied tremendously in the literature depending on the type of valve used (variation with valve generations and Self expanding/Balloon expanding valves). Our analysis reported an incidence of PPI to be 9.6% in BAV with supra-annular sizing. This incidence was similar to that reported from Society of Thoracic (STS)/American College of Cardiology (ACC) Transcatheter Valve Therapies (TVT) registry comprising of BAV subjects treated with annular size TAVR. The incidence of stroke as per our analysis was 6.9%, while registry consisting of BAV treated with annular sizing TAVR reported a stroke incidence of 2.4%.¹

There are several limitations for our analysis. All included trials and our meta-analysis do not have the required power for a sturdy

conclusion. The cardiac cycle and procedure used for measurements of the diameters are heterogeneous among studies. The studies reporting clinical outcomes following TAVR implantation with supra-annular size are few.

In conclusion, the present meta-analysis provides a pooled estimate of a treatment option of a rare entity. The analysis did not find a clinical significant difference in annular and supra-annular diameter. The incidence of PPI in our analysis was identical to the reported PPI among BAV subjects undergoing TAVR with annular sizing. Further trials studying the two sizing techniques in TAVR for BAV are required.

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Declaration of competing interest

None.

References

1. Chris SM, Patrick MM. *TAVR for bicuspid aortic valves: is surgery still the gold standard?* - *American College of Cardiology*; 2019. <https://www.acc.org/latest-in-cardiology/articles/2019/04/17/07/14/tavr-for-bicuspid-aortic-valves>. Accessed June 8, 2019.
2. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol*. 2014;14(1):135. <https://doi.org/10.1186/1471-2288-14-135>.
3. Luo D, Wan X, Liu J, Tong T. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. *Stat Methods Med Res*. 2016;27(6):1785–1805. <https://doi.org/10.1177/0962280216669183>.
4. Bax JJ, Delgado V, Bapat V, et al. Open issues in transcatheter aortic valve implantation. Part 1: patient selection and treatment strategy for transcatheter aortic valve implantation. *Eur Heart J*. 2014;35(38):2627–2638. <https://doi.org/10.1093/eurheartj/ehu256>.
5. Didier T, Chiara de B, Lennart van G, et al. Bicuspid aortic valve anatomy and relationship with devices: the BAVARD multicenter registry. *Circ Cardiovasc Interv*. 2019;12(1), e007107. <https://doi.org/10.1161/CIRCINTERVENTIONS.118.007107>.

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