

## Meta-analysis and meta-regression of early aortic valve replacement versus watchful waiting in asymptomatic severe aortic stenosis: a 2020 boost of evidence

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**Background:** Current guidelines recommend aortic-valve replacement (AVR) as the only effective therapy for severe symptomatic aortic stenosis (AS) patients. Nevertheless, management and timing of intervention in asymptomatic AS remains a controversial topic, with sparse evidence to support the recommendations (level C).

**Purpose:** To assess an early-AVR strategy in asymptomatic severe AS, comparing it with a watchful waiting (WW) strategy

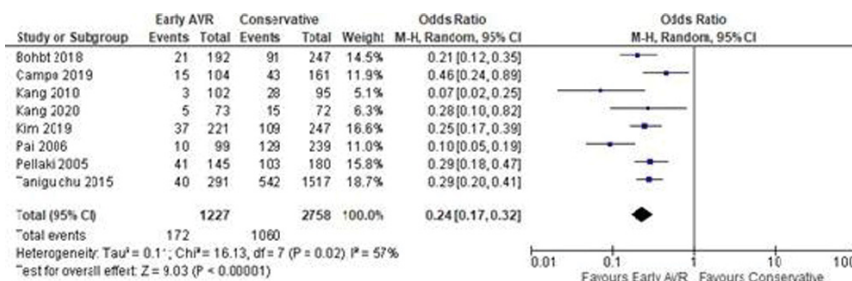
**Methods:** We systematically searched PubMed, Embase and Cochrane databases, in February 2020, for both interventional or observational studies comparing early-AVR with WW in the treatment of asymptomatic severe AS. Random-effects meta-analysis for early-AVR and WW were performed. Meta-regression was used to assess the influence of study characteristics on the outcome.

**Results:** Eight studies were included (seven registry-based or unrandomized studies and one randomized clinical trial) providing a total of 3985 patients, and 1232 pooled all-cause deaths (172 in early-AVR and 1060

in watchful waiting). Meta-analysis showed a significantly lower all-cause mortality for the early-AVR compared with WW group (pooled OR 0.24 [0.17, 0.32],  $P < 0.01$ ) although with a moderate amount of heterogeneity between studies in the magnitude of effect ( $I^2 = 57%$ ,  $P = 0.02$ ). The early-AVR patients also displayed a lower cardiovascular mortality (pooled OR 0.27 [0.15, 0.48],  $P < 0.01$ ) plus a lower heart failure hospitalization rate (pooled OR 0.27 [0.06, 0.65],  $P < 0.007$ ). No difference in clinical thromboembolic event rate (stroke or myocardial infarction) was noted.

The meta-regression for all cause mortality based on possible confounders such as time of follow-up, age, gender, diabetes mellitus, coronary artery disease, left ventricular ejection fraction, and mean peak aortic jet velocity showed that effect sizes reported by the individual studies seem to be independent from the covariates considered ( $P > 0.05$ ).

**Conclusions:** Our 2020 pooled data reinforces the previous evidence suggesting the benefit of early-AVR in asymptomatic patients with severe AS.



Early AVR vs WW, All-cause death