

F.5 Aortic stenosis – aortic valve calcium score on cardiac CT

Table 18: Clinical evidence profile: Aortic valve calcification on cardiac CT

Quality assessment							No of patients		Effect	Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Calcium score high	Calcium score normal	Relative (95% CI)	
Severe aortic valve calcification (≥ 2065 AU in men and ≥ 1274 in women) compared to non-severe aortic valve calcification (< 2065 AU in men and < 1274 AU in women) for predicting mortality under conservative treatment - adjusted HR (at least mild AS under conservative management) (follow-up mean 1.7 years)										
1	cohort studies	very serious ¹	no serious inconsistency	serious ²	no serious imprecision	none	410	384	HR 1.75 (1.04 to 2.93)	⊕○○○ VERY LOW

Severe aortic valve calcification (≥ 2065 AU in men and ≥ 1274 in women) compared to non-severe aortic valve calcification (< 2065 AU in men and < 1274 AU in women) for predicting death or AVR during follow-up - adjusted HR (AS of various severities and symptom status) (follow-up median 1029 days)										
1	cohort studies	very serious ¹	no serious inconsistency	serious ³	no serious imprecision	none	Not reported	Not reported	HR 3.8 (2.16 to 6.69)	⊕000 VERY LOW
≥ 723 compared to < 723 AU for predicting cardiac events - cardiac death, AVR, non-fatal myocardial infarction and HF requiring urgent hospitalisation - unadjusted (asymptomatic, mild to severe AS) (follow-up median 29 months)										
1	cohort studies	very serious ¹	no serious inconsistency	very serious ⁴	no serious imprecision	none	32	32	HR 6.08 (2.86 to 12.92)	⊕000 VERY LOW
≥ 723 compared to < 723 for predicting non-AVR cardiac events - cardiac death, non-fatal myocardial infarction and HF requiring urgent hospitalisation - unadjusted (asymptomatic, mild to severe AS) (follow-up median 29 months)										
1	cohort studies	very serious ¹	no serious inconsistency	very serious ⁴	no serious imprecision	none	32	32	HR 3.69 (1.39 to 9.82)	⊕000 VERY LOW
≥ 1266 vs < 1266 for predicting cardiac events - cardiac death, AVR, non-fatal myocardial infarction and HF requiring urgent hospitalisation - unadjusted (asymptomatic severe AS)										
1	cohort studies	very serious ¹	no serious inconsistency	very serious ⁵	serious ⁶	none	14	15	HR 1.71 (0.71 to 4.13)	⊕000 VERY LOW
≥ 1266 vs < 1266 for predicting non-AVR cardiac events - cardiac death, non-fatal myocardial infarction and HF requiring urgent hospitalisation - unadjusted (asymptomatic severe AS)										
1	cohort studies	very serious ¹	no serious inconsistency	very serious ⁵	serious ⁶	none	14	15	HR 3.08 (0.85 to 11.19)	⊕000 VERY LOW
$> 6,000$ HU vs $\leq 6,000$ HU for predicting rehospitalisation - adjusted HRs (undergoing TAVI) (follow-up 1 month post-TAVI) (follow-up 1 months)										
1	cohort studies	very serious ¹	no serious inconsistency	very serious ⁷	no serious imprecision	none	118		OR 23.24 (3.59 to 150.38)	⊕000 VERY LOW

>6,000 HU vs ≤6,000 HU for predicting all-cause mortality, stroke, myocardial infarction, heart failure or rehospitalisation for cardiac causes - adjusted HRs (undergoing TAVI) (follow-up 1 month post-TAVI)										
1	cohort studies	very serious ¹	no serious inconsistency	very serious ⁸	no serious imprecision	none	118		OR 106 (15.44 to 727.53)	⊕○○○ VERY LOW
>2027 compared to ≤2027 AU for predicting mortality post-AVR - 30 days - unadjusted (low-flow, low-gradient severe AS)										
1	cohort studies	very serious ¹	no serious inconsistency	serious ⁹	serious ⁶	none	10	11	HR 1 (0.1 to 10)	⊕○○○ VERY LOW
Calcium score ≥1200 vs <1200 in women and ≥2000 vs <2000 AU in men for predicting mortality post-TAVI - 1 year – adjusted (severe AS scheduled for TAVI)										
1	randomised trials	very serious ¹	no serious inconsistency	serious ¹⁰	serious ⁶	none	428	222	HR 1.32 (0.77 to 2.26)	⊕○○○ VERY LOW
Leaflet calcification >382 vs <382 mm³ for predicting all-cause mortality post-TAVI - 2 years – adjusted (severe AS with bicuspid valve scheduled for TAVI)										
1	randomised trials	serious ¹	no serious inconsistency	serious ¹¹	no serious imprecision	none	1034		HR 2.33 (1.41 to 3.85)	⊕⊕○○ LOW
Calcium density highest tertile vs moderate or low tertile for predicting mortality post-TAVI - 3 years – adjusted (severe low-flow, low-gradient AS)										
1	randomised trials	serious ¹	no serious inconsistency	serious ¹¹	no serious imprecision	none	98	192	HR 0.73 (0.6 to 0.89)	⊕⊕○○ LOW
Calcium density highest tertile vs moderate or low tertile in paradoxical LFLG AS for predicting mortality post-TAVI - 3 years – adjusted (severe paradoxical low-flow, low-gradient AS)										
1	randomised trials	serious ¹	no serious inconsistency	serious ¹¹	serious ⁶	none	79	157	HR 0.91 (0.73 to 1.13)	⊕○○○ VERY LOW
Leaflet calcification >382 vs <382 mm³ for predicting cardiovascular mortality post-TAVI - 2 years – adjusted (severe AS with bicuspid valve scheduled for TAVI)										

1	randomised trials	very serious ¹	no serious inconsistency	serious ¹¹	no serious imprecision	none	1034	HR 2.83 (1.38 to 5.8)	⊕000 VERY LOW
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¹ Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

² Population - unclear whether this represents a population where there was uncertainty about whether or not to intervene as includes mild-severe AS under conservative management

³ Outcome - composite outcome of two separate outcomes listed in the protocol, rather than reporting separately. Also unclear whether AVR captures only unplanned intervention as in our protocol, or whether some were planned procedures following CT results.

⁴ Population - unclear whether represents a population where there is uncertainty about whether or not to intervene, as includes mixture of mild-severe asymptomatic AS with only 45% severe; prognostic factor - threshold is quite different to that specified in the protocol and the same one has been used for men and women, rather than using a separate threshold; and outcome - composite outcome consisting of multiple outcomes listed in the protocol rather than reporting separately.

⁵ Prognostic factor - threshold is quite different to that specified in the protocol and the same one has been used for men and women, rather than using a separate threshold; and outcome - composite outcome consisting of multiple outcomes listed in the protocol rather than reporting separately.

⁶ 95% CI crosses null line

⁷ Population - all had TAVI so already an indication for intervention; and prognostic factor - threshold of 6,000 HU used very different to suggested thresholds in protocol and same one used for men and women.

⁸ Population - all had TAVI so already an indication for intervention; prognostic factor - threshold of 6,000 HU used very different to suggested thresholds in protocol and same one used for men and women; and outcome - composite outcome of multiple outcomes in protocol as well as some additional outcomes not listed in protocol

⁹ Prognostic factor - same threshold used for men and women rather than a separate one as in protocol

¹⁰ Population - all had TAVI so already an indication for intervention

¹¹ Population - all had TAVI so already an indication for intervention; and prognostic factor - calcium density, not calcium score threshold as stated in the protocol