F.2 Aortic stenosis – myocardial fibrosis on cardiac MRI

Table 15: Clinical evidence profile: myocardial fibrosis on cardiac MRI

Quality assessment							No of patients		Effect	Quality
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Myocardial fibrosis on cardiac MRI	Control	Relative (95% CI)	
Midwall fibrosis LGE pattern vs no LGE for predicting all-cause mortality (mixed medical/surgical treatment) - adjusted HR (moderate or severe AS) (follow-up mean 2.0 years)										
1	cohort studies	very serious[1]	no serious inconsistency	very serious[2]	no serious imprecision	none	54	49	HR 5.35 (1.17 to 24.56)	⊕OOO VERY LOW
Infarct fibrosis LGE pattern vs no LGE for predicting all-cause mortality (mixed medical/surgical treatment) - adjusted HR (moderate or severe AS) (follow-up mean 2.0 years)										
1	cohort studies	very serious[1]	no serious inconsistency	very serious[2]	serious[3]	none	40	49	HR 2.56 (0.48 to 13.65)	⊕OOO VERY LOW

Mild fibrosis compared to no fibrosis for predicting all-cause mortality following AVR - Adjusted for age and sex (symptomatic severe AS undergoing AVR) (follow-up 10 years 9 months (57/58 patients enrolled - 46 analysed for fibrosis))										
1	cohort studies	very serious[1]	no serious inconsistency	very serious[4]	serious[3]	none	Not reported	Not reported	HR 2.52 (0.6 to 10.66)	⊕OOO VERY LOW
Mild fibrosis compared to no fibrosis for predicting all-cause mortality following AVR - Adjusted for EuroSCORE (symptomatic severe AS undergoing AVR) (follow-up 10 years 9 months (57/58 patients enrolled - 46 analysed for fibrosis))										
1	cohort studies	very serious[1]	no serious inconsistency	very serious[4]	serious[3]	none	Not reported	Not reported	HR 2.98 (0.74 to 11.96)	⊕OOO VERY LOW
Severe fibrosis vs no fibrosis for predicting all-cause mortality following AVR - Adjusted for age and sex (symptomatic severe AS undergoing AVR) (follow-up 10 years 9 months (57/58 patients enrolled - 46 analysed for fibrosis))										
1	cohort studies	very serious[1]	no serious inconsistency	very serious[4]	no serious imprecision	none	Not reported	Not reported	HR 6.03 (1.66 to 21.91)	⊕OOO VERY LOW
Severe fibrosis vs no fibrosis for predicting all-cause mortality following AVR - Adjusted for EuroSCORE (symptomatic severe AS undergoing AVR) (follow-up 10 years 9 months (57/58 enrolled - 46 analysed for fibrosis))										
1	cohort studies	very serious[1]	no serious inconsistency	very serious[4]	serious[3]	none	Not reported	Not reported	HR 3.7 (0.93 to 14.72)	⊕OOO VERY LOW
LGE vs no LGE for predicting all-cause mortality and unexpected hospitalisation for HF during follow-up (mixed medical and surgical treatment) - adjusted HR (moderate or severe AS) (follow-up median 27.9 months)										
1	cohort studies	very serious[1]	no serious inconsistency	very serious[5]	no serious imprecision	none	41	86	HR 1.56 (1.05 to 2.32)	⊕OOO VERY LOW
Fibrosis vs no fibrosis for predicting unplanned hospital admission (for AF, HF or ACS), aortic valve replacement or death - adjusted HR (asymptomatic severe AS) (follow-up median 358 days[6])										
1	cohort studies	very serious[1]	no serious inconsistency	serious[7]	serious[3]	none	21	57	HR 1.17 (0.44 to 3.11)	⊕OOO VERY LOW

LGE vs no LGE for predicting mortality, LVEF drop ≥2, new-onset HF or hospitalisation for cardiovascular causes and new-onset arrythmia (mixed medical/surgical treatment) - adjusted HR (severe AS) (follow-up mean 13 months)										
1	cohort studies	very serious[1]	no serious inconsistency	very serious[8]	serious[3]	none	46	63	OR 1.68 (0.60 to 4.6)	⊕OOO VERY LOW
LGE vs no LGE for predicting major adverse cardiac events - sudden cardia death, non-fatal myocardial infarction, sustained ventricular arrhythmias, third-degree AV block and hospitalisation for HF - adjusted HR (severe AS having AVR) (follow-up median 386 days)										
1	cohort studies	serious[1]	no serious inconsistency	very serious[9]	no serious imprecision	none	30	22	HR 11.3 (1.82 to 70.18)	⊕OOO VERY LOW
LGE vs no LGE for predicting all-cause mortality post-intervention - adjusted HR (severe AS having valve intervention) (follow-up median 2.9-3.8 years)										
3	cohort studies	very serious[1]	no serious inconsistency	serious[10]	no serious imprecision	none	605	602	HR 1.94 (1.34 to 2.8)	⊕OOO VERY LOW
LGE vs no LGE for predicting cardiovascular mortality post-intervention - adjusted HR (severe AS having valve intervention) (follow-up median 3.6 years)										
1	cohort studies	serious[1]	no serious inconsistency	serious[10]	no serious imprecision	none	341	272	HR 3.14 (1.65 to 5.98)	⊕⊕OO LOW
Diffuse myocardial fibrosis vs normal myocardium for predicting cardiovascular death, hospitalisation for cardiac causes, non-fatal stroke and symptomatic aggravation (worsening NYHA class) following AVR - adjusted HR (severe AS undergoing AVR) (follow-up median 38.8 months)										
1	cohort studies	very serious[1]	no serious inconsistency	very serious[11]	no serious imprecision	none	30	13	HR 5.52 (1.03 to 29.51)	⊕OOO VERY LOW

[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 indication for intervention was unclear in all patients, as includes some that underwent AVR which may have been scheduled prior to CMR; prognostic factor - provides results separately for two types of LGE on CMR rather than as a single combined result vs. no LGE on CMR; and outcome - includes those with and without surgery during follow-up, whereas ideally aimed to look at results for operative and non-operative mortality separately
[3] 95% CI crosses null line
[4] Population - all were symptomatic severe AS undergoing AVR, so already have an indication for intervention prior to CMR; and prognostic factor - specific severity of fibrosis on CMR compared with no fibrosis rather than comparing any fibrosis with no fibrosis

[5] Population - includes a large proportion that were already deemed to have an indication for intervention regardless of CMR results; and outcome - composite outcome of multiple outcomes in protocol combined rather than reported separately. Also includes those with and without operation in the analysis, whereas ideally aimed to analyse operative and non-operative outcomes separately.
[6] This was for the whole cohort of 92 patients and not limited to the 72 included in fibrosis analysis
[7] Outcome - composite of three separate outcomes listed in the protocol rather than reporting them separately
[8] Population - 35% already deemed to have indications for intervention regardless of CMR results; and outcome - composite of multiple factors listed in protocol, as well as some not listed in protocol, rather than reporting separately. Also includes medically managed and surgically managed patients in the same analysis, whereas ideally aimed to analyse postoperative and non-operative outcomes separately.
[9] Population - indication for intervention already present as population was severe AS patients undergoing AVR; and outcome - composite of multiple outcomes including some of those in protocol as well as additional ones
[10] Population - all already scheduled for AVR so does not represent population where there is uncertainty about whether or not intervention is indicated
[11] Population - all already scheduled for AVR so no uncertainty as to whether there is an indication for intervention prior to CMR; and outcome - composite of multiple outcomes in the protocol combined rather than reported separately