D.6 Aortic regurgitation – regurgitant fraction and volume on cardiac MRI

Reference	Kockova 2019[140]
Study type and analysis	Prospective cohort study Multivariable Cox proportional hazards regression model
Number of participants and characteristics	**Total n=104** 3 failed to complete the MRI because of claustrophobia or spine deformity CMR-derived regurgitant volume <45 (n=?) and ≥45 ml (n=?). CMR-derived regurgitant fraction <34% (n=?) and ≥34% (n=?).

Reference	Kockova 2019[140]
	Inclusion criteria (1) severe AR defined by using the integrative 2D ECHO approach; (2) absence of symptoms validated using bicycle ergometry; (3) preserved LVEF (>50%); (4) non-dilated LV end-diastolic diameter (≤70 mm) and LV end-systolic diameter index (≤25 mm/m^2); and (5) sinus rhythm. **Exclusion criteria** Guideline indications for AV intervention, acute AR, aortic dissection, endocarditis, irregular heart rate, associated with more than mild valvular disease, complex congenital heart disease, intracardiac shunt, creatinine clearance <30 mL/min, pregnancy, or contra indication for MRI **Values listed below are presented as mean (SD), median (IQR) or number (%)** **Patient characteristics:** Age: 44 (13) years Male (%) 86% Smoker (%) 13% CAD 4% NYHA class I (%) 100% Systolic blood pressure, mmHg: 136 (16) LVEF on 2D echo 64 (6)% Moderate-to-severe AR 54% Severe AR 46% **Population source**: Consecutive patients from three tertiary cardiology centres Enrolment from March 2015 to September 2018; follow up assessment every 6 months to 30 September 2018 Median follow-up of 587 days (IQR) 296–901 days, The follow-up data on AV interventions, mortality, and cardiac hospitalizations were obtained in all patients (100%) using population registry, medical files, and contact with referring physicians or family.
Prognostic variable	CMR-derived regurgitant volume ≥45 ml vs <45 CMR-derived regurgitant fraction ≥34% vs <34
Confounders	MRI-derived LV volumes or their indices.

Reference	**Kockova 2019[140]**
Outcomes and effect sizes	Aortic valve surgery 0 deaths occurred A total of 20 (19%) individuals underwent AV surgery while the remaining patients were treated conservatively. **Adjusted hazard ratios for event-free survival** 1.03 (1.01−1.04) for RV ≥45 ml vs <45 on CMR 1.05 (1.02−1.08) for RF ≥34% vs <34 on CMR
Comments	Risk of bias: 1. Study participation LOW 2. Study attrition LOW 3. Prognostic factor measurement LOW 4. Outcome Measurement HIGH 5. Study confounding HIGH 6. Statistical analysis LOW 7. Other risk of bias LOW OVERALL RISK OF BIAS VERY HIGH Indirectness: • None identified

Reference	**Myerson 2012[191]**
Study type and analysis	Retrospective cohort study Multivariable Cox proportional hazards regression model and multiple logistic regression
Number of participants	**Total n=113** Aortic regurgitant fraction measured by CMR ≤33% (n=74) and >33% (n=39), (scan with highest regurgitant fraction used as the baseline).

Reference	Myerson 2012[191]
and characteristics	CMR-derived regurgitant volume ≤42 (n=?) and >42 ml (n=?). **Inclusion criteria** Patients at least 18 years of age, asymptomatic with moderate or severe chronic AR on echocardiography by standard (semi-quantitative) assessment **Exclusion criteria** Presence of other significant valve disease or clinical or angiographic evidence for coronary disease **Values listed below are presented as mean (SD), median (IQR) or number (%)** **Patient characteristics:** **Conservative Mx** / **Requiring surgery** Age: 50.8 (16.8) years / 45.7 (18.7) Systolic blood pressure, mmHg: 132.9 (19.3) / 134.2 (16.0) LVEF: 63.6 (8.7) % / 62.9 (6.4)% Regurgitant volume (ml): 27.5 (15.5) / 74.7 (28.5) Regurgitant fraction (%) 21.8 (9.8) / 42.0 (9.5) **Population source**: 4 high-volume CMR centres in Oxford, London, Leeds (United Kingdom), and Auckland (New Zealand). Time frame for sampling unclear Follow up was up to 9 years (mean 2.6±2.1 years) In Oxford, patients participated in a research study, with annual CMR scans, and clinical decisions were made without knowledge of the CMR data. In the other 3 centres study patients were identified from the clinical CMR databases (although they were initially diagnosed with echocardiography) and clinicians had access to the CMR data.
Prognostic variable	Aortic regurgitant fraction measured by CMR >33% (n=39) vs ≤33% (n=74) CMR-derived regurgitant volume >42 ml (n= not reported) vs ≤42 (n= not reported).
Confounders	Unclear, likely RF, RV and LVEDV
Outcomes and effect sizes	Thirty-nine patients (35%) underwent aortic valve replacement during the follow-up period, having developed symptoms (n=19) or other established echocardiographic indications for surgery (excessive LV dilation, n=17; or reduced LV function [echocardiographic

Reference	Myerson 2012[191]
	ejection fraction <50%], n=3). RF ≤33% survival 93% RF >33% survival 34% **Adjusted hazard ratios for indication for developing indication for surgery (initially asymptomatic)** 7.4 (3.0 to 18.6) for RF >33% vs ≤33 on CMR 13.2 (3.8 to 45.8) for RV >42 on vs ≤42 CMR Events were only counted if the reason for aortic valve surgery was for established indications (primarily symptoms, excess LV dilation, or LV dysfunction). A minimum period of 2 months was required between the CMR scan and the decision for surgery to avoid the potential bias of patients having a CMR scan en route to surgery that had already been planned.
Comments	Risk of bias: 1. Study participation HIGH 2. Study attrition LOW 3. Prognostic factor measurement LOW 4. Outcome Measurement HIGH 5. Study confounding HIGH 6. Statistical analysis LOW 7. Other risk of bias LOW OVERALL RISK OF BIAS VERY HIGH Indirectness: • None identified