D.7 Mitral regurgitation – regurgitant volume on cardiac MRI

Reference	Myerson 2016[190]
Study type and analysis	Prospective cohort study Cox proportional hazards regression model
Number of participants and characteristics	**Total n=109** Censored at the point of surgery CMR-derived regurgitant volume ≤55 (n=80) and >55 ml (n=29). CMR-derived regurgitant fraction ≤40% (n=67) and >40% (n=42). **Inclusion criteria** Asymptomatic patients with moderate or severe chronic organic mitral regurgitation on echocardiography **Exclusion criteria** 'Functional' mitral regurgitation (secondary to annular dilation or LV dysfunction), other significant valve disease and clinical and/or angiographic evidence of coronary disease. **Values listed below are presented as mean (SD), median (IQR) or number (%)** **Patient characteristics:** **Conservative Mx (n=84)** / **Requiring surgery (n=25)** Age (years): 65.1 (14.9) / 63.8 (12.6) Male (%) 65 / 76 Systolic blood pressure, mmHg: 143.9 (23.1) / 132.1 (20.1) LVEF: 66.9 (7.6)% / 63.9 (7.4)% Regurgitant volume (ml): 39.4 (20.0) / 65.9 (23.7) Regurgitant fraction (%) 32.1 (12.4) / 45.7 (11.7) **Population source**: Consecutive patients from four high-volume CMR centres in Oxford, Leeds, London (UK) and Auckland (New Zealand). Recruitment period unclear

Reference	**Myerson 2016[190]**
	Follow up was up to 8 years (mean 2.5 ± SD 1.9 years; median 1.6 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	CMR-derived regurgitant volume ≤55 (n=80) and >55 ml (n=29). CMR-derived regurgitant fraction ≤40% (n=67) and >40% (n=42).
Confounders	N/A
Outcomes and effect sizes	Indication for surgery Twenty five patients (23%) underwent mitral valve repair/replacement during the follow-up period (the 'crossover' group), having developed symptoms (n=19) or other established echocardiographic indications for surgery (excessive LV dilation [ESD >4.0cm], n=4; or pulmonary hypertension [>50mmHg] with a repairable valve, n=2) Subjects with a regurgitant volume <55ml had a very high chance of remaining free of symptoms or surgery: 95% at the median time (1.6 years) and 91% at 5 years. This contrasted with 54% at 1.6 years and 21% at 5 years for patients with regurgitant volume >55m **Unadjusted hazard ratios for indication for surgery up to 5 years** 0.20 (0.09−0.45) for RV ≤55 vs >55 ml on CMR Unable to calculate HR for RF because data divided into three subgroups 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

Reference	Myerson 2016[190]	
	6. Statistical analysis	LOW
	7. Other risk of bias	LOW
	OVERALL RISK OF BIAS	VERY HIGH
	Indirectness: • None identified	

Reference	Penicka 2018[213]
Study type and analysis	Prospective cohort study Cox proportional hazards regression model
Number of participants and characteristics	**Total n=258** Numbers in different regurgitant volume categories not available **Inclusion criteria** 1) absence of symptoms, validated using a bicycle exercise test; (2) preserved left ventricular (LV) ejection fraction (>60%) using the biplane Simpson method; and (3) sinus rhythm. **Exclusion criteria** Mild or no OMR, presence of symptoms, reduced LV ejection fraction (≤60%), non-sinus rhythm, history of coronary artery disease, concomitant aortic regurgitation, intracardiac shunt, contraindication for MRI, and poor echocardiography image quality **Values listed below are presented as mean (SD), median (IQR) or number (%)** **Patient characteristics:** **Age:** 63 (14) years Male (%): 60 **Regurgitant volume on** MRI (ml): 55.7 **Population source**: Consecutive patients from 2 centres in Belgium and Czech Republic. Recruitment period January 2011 to December 2014

Reference	Penicka 2018[213]
	Follow up median 5.0 years (IQR 3.5–6.0 years) Clinical decisions were made without knowledge of the CMR data. Analysis was performed by an operator blinded to the results of echocardiographic assessment and the symptomatic status of the patient.
Prognostic variable	CMR-derived regurgitant volume (continuous variable: per 10ml increase)
Confounders	Age, sex and MRI-derived LVESVI
Outcomes and effect sizes	Indication for surgery The recommended indications for mitral valve surgery at the time of the study included development of symptoms, LV dysfunction (LV end-systolic diameter ≥45 mm or LV ejection fraction ≤60%), and new onset of atrial fibrillation or pulmonary hypertension (systolic pulmonary artery pressure >50 mm Hg at rest). However, the final decision whether to refer a patient for surgery was taken by the referring cardiologist together with the patient and GP. 38 (15%) patients died, 58 (22%) underwent mitral valve surgery, and 106 (41%) either died or developed indication for mitral valve surgery. **Adjusted hazard ratio for all-cause mortality** 1.10 (1.05–1.20) for RV on CMR **Adjusted hazard ratio for indication for mitral valve surgery** 1.23 (1.06–1.29) for RV on CMR According to the Youden index, the optimal cut-off of RV to predict mortality and its combination with the development of indication for mitral valve surgery was ≥50 mL.
Comments	Risk of bias (both outcomes): 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

Reference	Penicka 2018[213]
	7. Other risk of bias LOW OVERALL RISK OF BIAS VERY HIGH Indirectness: • Prognostic factor indirectness: only reported as a continuous variable