# Prognostic Value of Delayed Enhancement Cardiac Magnetic Resonance Imaging in Mitral Valve Repair

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Background. The objective of this study was to examine the prognostic utility of cardiac magnetic resonance imaging (CMR) in patients with chronic mitral regurgitation undergoing mitral valve repair.

Methods. This study is a prospectively enrolled observational cohort study of 48 consecutive patients with chronic mitral regurgitation who had preoperative evaluation with CMR including delayed-enhancement CMR for assessment of myocardial fibrosis before undergoing mitral valve repair. Postoperative adverse clinical events were defined as intensive care unit readmission, needs of permanent cardiac pacemaker, and rehospitalization for cardiac reasons.

Results. The cohort comprised 33 (69%) men with a mean age of  $61 \pm 13$  years and mean left ventricular ejection fraction of  $0.63 \pm 0.12$ . Preoperative myocardial fibrosis was detected in 40% of the patients. Median fibrosis was 4% (interquartile range, 2% to 10%). Mean follow-up duration was 11 months (interquartile range,

1 to 24 months). Adverse clinical events occurred in 16 patients. In multivariate analysis, the presence of myocardial fibrosis was independently associated with postoperative adverse clinical events (hazard ratio, 4.775; 95% confidence interval, 1.100 to 20.729; p=0.037). The addition of the presence of myocardial fibrosis to the preoperative characteristics model significantly improved overall predictive performance (p=0.04).

Conclusions. The presence of preoperative myocardial fibrosis assessed with delayed-enhancement CMR was an independent predictor of increased adverse clinical outcomes in patients with chronic mitral regurgitation undergoing mitral valve repair. Our findings suggest that in this population, preoperative delayed-enhancement CMR may be of clinical utility.

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The role of cardiac magnetic resonance (CMR) has been well established for the assessment of chronic mitral regurgitation (MR). In this role it is able to provide quantitative assessment of MR severity, insights into the mechanism of regurgitation, and an assessment of the consequences of the regurgitant lesion on left ventricular (LV) volumes and systolic function [1]. In recent years delayed-enhancement CMR (DE-CMR) has become a robust application for detection of LV myocardial fibrosis [2]. Cardiac magnetic resonance—derived myocardial fibrosis assessment has been shown to be a vigorous predictor of adverse clinical outcomes in numerous cardiovascular patient populations [3–6].

In a cardiac surgery arena, the presence of preoperative myocardial fibrosis by DE-CMR has been extensively examined in patients undergoing coronary artery bypass graft surgery. Myocardial fibrosis identified by DE-CMR before coronary artery bypass grafting has demonstrated the ability to predict functional improvement [7],

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LV remodeling [8], and adverse clinical events postoperatively [9]. However, despite substantial evidence of CMR-derived myocardial fibrosis as a prognosticator in patients undergoing different cardiac surgeries, the role of CMR in patients with chronic MR undergoing mitral valve repair (MVREP) has never been specifically elucidated to date.

Our hypothesis was that patients with chronic MR who had myocardial fibrosis detected by DE-CMR preoperatively would have increased adverse clinical events after MVREP surgery. This pilot study was aimed at investigating the prognostic performance of preoperative myocardial fibrosis in the LV by DE-CMR in patients with chronic severe MR who underwent MVREP.

#### Material and Methods

Study Design

This is a prospectively enrolled observational cohort study designed to examine the prognostic utility of myocardial fibrosis detected with DE-CMR in patients with chronic MR undergoing MVREP. Our cohort was consecutive patients with severe chronic MR who

#### Abbreviations and Acronyms

CAD = coronary artery disease

CMR = cardiac magnetic resonance imaging

DE-CMR = delayed-enhancement CMR

ICU = intensive care unit IQR = interquartile range

LV = left ventricle/left ventricular

MR = mitral regurgitation MVREP = mitral valve repair

underwent CMR imaging before MVREP between November 2008 and March 2013. All enrolled patients underwent MVREP with a nonresectional dynamic technique by one experienced cardiac surgeon [10]. Institutional review board approval was obtained for this study.

### Cardiac Magnetic Resonance Imaging Acquisition Protocol

Cardiac magnetic resonance imaging was performed with either 1.5-T or 3.0-T clinical scanners (Siemens Avanto and Siemens Verio; Siemens, Erlangen, Germany) with phased-array coil systems. A standard CMR examination consisted of the following: cine-CMR was performed for anatomic and functional assessment using a steady-state free-precession sequence with typical repetition time, 3.0 ms; echo time, 1.5 ms; in-plane spatial resolution, 1.7 to  $2.0 \times 1.4$  to 1.6 mm; slice thickness, 6 mm; temporal resolution, 35 to 40 ms.

Assessment of the mechanism of MR was performed by evaluating the cine-CMR images that were acquired in standard three-chamber, four-chamber, and "en-face" views of the MV as well as a stack of three chambers acquired to visualize individual scallops (A1–P1, A2–P2, and A3–P3) [11]. The MR mechanism was classified as either primary or secondary. Primary MR was defined as a valve lesion caused by primary dysfunction in the leaflets, such as leaflet prolapse or flail. Secondary MR was defined as a valve dysfunction caused by leaflet tethering as a result of a dilated LV or related to a wall motion abnormality in anatomically normal leaflets [11].

Left ventricular and right ventricular volumes were measured by planimetry of the endocardial borders on a stack of short-axis images acquired from breath-hold steady-state free-precession cines covering both ventricles, from base to apex, 1 slice per breath hold. Papillary muscles and trabeculae were excluded from the blood pool on the contours. Left ventricular end-diastolic volume, LV end-systolic volume, right ventricular end-diastolic volume, and right ventricular end-systolic volume were calculated by summation of these images. Left ventricular ejection fraction and right ventricular ejection fraction were determined by subtracting the end-systolic volumes from the end-diastolic volumes and dividing the result by end-diastolic volumes.

Delayed-enhancement CMR was performed for tissue characterization using a segmented inversion-recovery sequence [12] (in-plane spatial resolution,  $1.8 \times 1.3$  mm;

slice thickness, 6 mm; temporal resolution, 160 to 200 ms) 10 to 15 minutes after intravenous contrast administration (gadopentetate dimeglumine, 0.125 mmol/kg). Cine- and DE-CMR images were obtained in matching short- and long-axis planes. Short-axis images were acquired every 1 cm (gap, 4 mm) throughout the entire LV. Long-axis images were obtained in standard two-, three-, and four-chamber orientations.

For DE-CMR, inversion times were adjusted to null viable myocardium [13]. Coronary artery disease (CAD) -related fibrosis was defined as DE that was present subendocardially or transmurally in the myocardium following a coronary artery distribution [14]. Non-CAD fibrosis was defined as DE that was not localized in the subendocardium and did not follow a coronary distribution [15]. Fibrosis burden was quantified as percentages using the American Heart Association 17-segments LV model as described previously [16].

#### Data Collection and Clinical Events

Patient information including baseline demographics, comorbidities, and medications was collected at the time of the scan. Preoperative and early postoperative echocardiographic information was collected using the echocardiogram closest to the time of MVREP if there was more than one. History of CAD was defined by the presence of obstructive stenosis of at least one major epicardial vessel on selective coronary angiography, which was performed during the preoperative workup.

After MVREP, postoperative hospital courses and follow-up cardiac events were gathered by review of inpatient and outpatient medical records. The adverse clinical end point in our study was a composite of intensive care unit (ICU) readmission after MVREP, need for permanent pacemaker placement, and rehospitalization for cardiac reasons. If the patients had more than one adverse clinical event, only one was counted toward the end point. Decision for ICU readmission was made by the patients' medical teams, which were composed of cardiac surgeons, cardiologists, and cardiac intensivists. Need of permanent pacemaker included all permanent pacemaker placement occurring after MVREP. Cardiac rehospitalization was defined as rehospitalization after the index admission for MVREP for cardiac reasons including bradyarrhythmia, pulmonary edema, atrial fibrillation, and postpericardiotomy syndrome.

#### Statistical Analysis

Descriptive statistics for studied variables are presented as mean  $\pm$  standard deviation for normally distributed continuous variables, including age and all echocardiographic and CMR variables. Nonnormally distributed continuous variables are presented as median and interquartile range (IQR), including LV myocardial fibrosis and body mass index. Frequency with percentage is used for categorical variables.

Independent Student's t test was used to identify differences in means between two groups. Wilcox-Mann-Whitney U test was used to examine differences in medians. The  $\chi^2$  analysis or Fisher's exact test was used to

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