Tethering Symmetry Reflects Advanced Left Ventricular Mechanical Dyssynchrony in Patients With Ischemic Mitral Regurgitation Undergoing Restrictive Mitral Valve Repair

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Background. **We evaluated the papillary muscle systolic dyssynchrony (DYS-PAP) using two-dimensional speckle tracking echocardiography (2D-STE) in patients with chronic ischemic mitral regurgitation (CIMR) showing different preoperative leaflet pattern and investigated the impact of baseline tethering pattern in the prediction of significant post-repair desynchronized papillary muscle contraction.**

Methods. **We recruited 152 CIMR consecutive patients (64.4% male, mean age 65.9 ± 7.1 years) who survived coronary artery bypass grafting (CABG) and (undersized mitral ring annuloplasty, performed between 2001and 2010. The assessment of DYS-PAP was performed preoperatively and at follow-up (median 41.5 months [IQR 23–61]) by 2D-STE in the apical 4-chamber view for anterolateral papillary muscle and apical long-axis view for posteromedial papillary muscle). Based on the cutoff value (anterior-posterior tethering angle ratio $\alpha/\beta \geq 0.76$) patients were classified in 2 groups; symmetrical (group 1, n = 73, mean $\alpha/\beta = 0.81 \pm 0.6$) and asymmetrical preoperative tethering pattern (group 2, n = 79, mean $\alpha/\beta = 0.66 \pm 0.4$).**

Results. **Recurrent MR occurred in 67.1% (n = 49) in group 1 versus 3.8% (n = 3) in group 2 ($p < 0.001$). Comparing both groups at baseline, patients in group 1 had higher DYS-PAP (57.7 ± 5.3 vs 29.8 ± 2.4 ms in group 2, $p < 0.001$) that significantly worsened at follow-up (78.1 ± 8.8 ms, $p < 0.001$ versus baseline), whereas in group 2 it improved (26.6 ± 6.0 ms, $p < 0.001$ versus baseline). Tethering symmetry significantly correlated with DYS-PAP (r = 0.90, $p < 0.001$) and it was a strong multivariable predictor of significant postoperative DYS-PAP (odds ratio 4.2; 95% confidence level 3.4 to 5.2, $p < 0.001$).**

Conclusions. **Tethering symmetry is an easy and immediate tool to identify CIMR patients with advanced DYS-PAP who are unlikely to benefit from mitral repair with undersized mitral ring annuloplasty.**

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Chronic ischemic mitral regurgitation (CIMR) remains one of the most complex and unresolved aspects of ischemic heart disease because of the unsatisfactory results of current strategies [1, 2]. Chronic ischemic mitral regurgitation is becoming the focus of an increasing amount of cardiovascular research mainly focused on better understanding pathophysiologic mechanisms underlying CIMR and their impact on postoperative results [3]. In particular, more attention has been drawn to the preoperative tethering pattern to predict MR recurrence after undersizing mitral ring annuloplasty (UMRA) and to establish whether a specific preoperative leaflet configuration is related to unfavorable outcomes [4–6].

Recent evidence suggests that dyssynchronous papillary muscle activation may be a contributing factor in functional mitral regurgitation [7] and it has been reported to be useful in detecting subclinical deterioration in left ventricular (LV) function [8]. Nonetheless, no information exists about papillary muscle systolic dyssynchrony (DYS-PAP) in CIMR and little is known about the relationship between DYS-PAP and tethering pattern in CIMR patients, and whether the persistence of dyssynchronous papillary muscle activation might be related to a specific leaflet configuration.

In this study we evaluated the DYS-PAP with two-dimensional speckle tracking echocardiography in CIMR patients and we investigated the impact of baseline tethering pattern on the prediction of significant post-repair desynchronized papillary muscle contraction.

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Abbreviations and Acronyms

2D-STE	= two-dimensional speckle tracking echocardiography
ALPM	= anterolateral papillary muscle
ALPM-LS	= anterolateral papillary muscle longitudinal strain
CD	= coaptation distance
CH	= coaptation height
CIMR	= chronic ischemic mitral regurgitation
CL	= coaptation length
DSI	= diastolic sphericity index
DYS-PAP	= papillary muscle dyssynchrony
EDD	= end diastolic diameter
EDVI	= end diastolic volume index
EROA	= effective regurgitant orifice area
ESD	= end systolic diameter
ESVI	= end systolic volume index
G-LS	= global longitudinal strain
LVEF	= left ventricular ejection fraction
MPI	= myocardial performance index
PMPM	= posteromedial papillary muscle
PMPM-LS	= posteromedial papillary muscle longitudinal strain
RF	= regurgitant fraction
RV	= regurgitant volume
SSI	= systolic sphericity index
TA	= tenting area
UMRA	= undersized mitral ring annuloplasty
WMSI	= wall motion score index
α	= anterior mitral leaflet tethering angle
β	= posterior mitral leaflet tethering angle

Material and Methods

Subjects

The Ethics Committee approved the study and waived the need for patient consent according to the national law regulating observational retrospective studies (Dutch WMO law). However, all patients gave their informed consent to access their data for scientific purposes. We retrospectively evaluated patients with CIMR referred to our Institution (University Hospital of Maastricht, Maastricht, The Netherlands) by 7 satellite hospitals (Heerleen, Helmond, Kerkrade, Roermond, Sittard, Venlo, Weer, The Nederlands) between 2001 and 2010.

Inclusion criteria were the following [6, 9]: (1) mild-to-severe MR with prior myocardial infarction >16 days; (2) 75% or greater stenosis of at least 1 coronary vessel; (3) a corresponding regional wall motion abnormality; and (4) restricted-motion type leaflet dysfunction with or without annular dilatation. Exclusion criteria were the following: (1) mitral valve replacement; (2) death; (3) persistent or residual MR (MR $\geq$ moderate at discharge); (4) degenerative or other nonischemic etiology; (5) acute ischemic MR; (6)additional mitral valve repair procedures; (7) other valvular or congenital heart diseases; (8) previous cardiac surgery or percutaneous transluminal coronary angioplasty; (9) atrial fibrillation (10) incomplete or unavailable echoes for strain analysis. The final study population consisted of 152 CIMR patients (Fig 1). Recurrence of MR was defined as insufficiency greater than or equal to moderate (in patients with no or trivial MR at discharge) at the last echocardiographic control performed at a median of 41.5 months (interquartile range 23 to 61).

Surgery

Patients with moderate or severe CIMR (effective regurgitant orifice area > 20 mm^2 and regurgitant volume > 30 mL) were scheduled for operation. When MR was moderate, surgery was indicated in the presence of a dilated left ventricle (end-diastolic volume > 110 mL/m^2) or low LV ejection fraction (< 0.35), as in the case of dilated cardiomyopathy [10]. All patients underwent complete revascularization. Mitral annuloplasty was performed with standard operative techniques, including cardiopulmonary bypass and undersized annuloplasty rigid ring placement (Carpentier-Edwards Classic; Edwards LifeSciences, Irvine, CA). The ring size was determined by standard measurements of the intertrigonal distance and anterior leaflet height. Downsizing by 2 ring sizes was performed in all patients. A successful repair was assessed as leaflet coaptation of 0.8 cm or more, MR of 1 or less, and a systolic mitral valve area exceeding 2 cm^2 at intraoperative transesophageal echocardiography.

Echocardiography

Transthoracic echocardiography was performed after a common standard protocol at baseline (within a week before surgery), at discharge, 6 months, and at yearly follow-up visits. Exams were carried out using a commercially available ultrasound system, IE 33 (Philips Medical System, Amsterdam, The Netherlands). Images were stored in Digital Imaging and Communications in Medicine format and transferred to a workstation for further offline analysis (Tomtec Imaging system, Unterschleiβheim, Germany). Measurements and calculations were made separately by one of the investigators (F.L.). Echocardiographic measurements and calculations were carried out as previously reported [9].

The severity of MR was graded on a scale of 1 to 4 according to American Society of Echocardiography Guidelines [11]. In patients with no or trivial MR by color Doppler, regurgitant volume, and regurgitant fraction were used as calculated, and effective regurgitant orifice area was assumed as null.

Left ventricular volumes and LV ejection fraction were assessed using the biapical Simpson disk method [12]. Sphericity indexes were obtained at end-diastole and end-systole as the volume of the LV divided by the volume of a sphere with a diameter equal to the longest axis of the LV measured in the apical view [13]. The wall motion score index (WMSI) was calculated according to a 17-segment model. The WMSI of the basal and mid-posterior and inferior segments for the posteromedial papillary muscle (PMPM-WMSI) and basal-mid-lateral and anterior segments for the anterolateral papillary muscle (ALPM-WMSI) were also calculated [14]. The