Importance of anterior leaflet tethering in predicting recurrence of ischemic mitral regurgitation after restrictive annuloplasty

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Objective: We investigated the relationship between anterior mitral leaflet (AML) tethering and recurrent ischemic mitral regurgitation (MR) after restrictive annuloplasty. We also explored whether the effect of AML tethering was secondary to modifications in left ventricular size and geometry.

Methods: The study population consisted of 435 consecutive patients with chronic ischemic MR who survived combined coronary artery bypass grafting and undersized mitral ring annuloplasty performed at 3 institutions (University Hospital, Maastricht, The Netherlands; Careggi Hospital, Florence, Italy; and Civic Hospital, Brescia, Italy) from 2001 to 2008. The median follow-up was 44.7 months (interquartile range 25.9–66.4). The patients were divided by the baseline measurements into quintiles of AML tethering angle α' as follows: group 1, normal/slight AML tethering; group 2, mild AML tethering; group 3, moderate AML tethering; group 4, moderate-to-severe AML tethering; and group 5, severe AML tethering.

Results: Recurrence of MR was significantly greater in patients with moderate-to-severe (28.3%) and severe (39.4%) AML tethering ($P < .001$). A strong correlation was found between α' ($r = 0.83$, $P < .001$) and recurrent MR but a weak correlation with the posterior mitral angle β' ($r = 0.12$, $P = .05$). On logistic regression analysis corrected for other echocardiographic risk factors, moderate-severe AML tethering or worse (adjusted odds ratio, 3.6; 95% confidence interval, 3.0–4.1; $P < .001$) was a strong predictor of MR recurrence. Compared with patients with β' of 45 or greater, those with severe and moderate-severe AML tethering had more than 3.7 and 1.7 times greater odds of MR recurrence, respectively. No significant interactions were found between α' and the indexes of left ventricular function and geometry.

Conclusions: Preoperative moderate-severe AML tethering or worse was strongly associated with MR recurrence. Thus, assessment of leaflet tethering should be incorporated into clinical risk assessment and prediction models. (J Thorac Cardiovasc Surg 2012;143:S54-9)

Despite undersized mitral ring annuloplasty (UMRA) being considered effective for chronic ischemic mitral regurgitation (MR),[1] ongoing dissatisfaction with MR recurrence has been reported predominantly related to continued adverse left ventricular (LV) remodeling and ensuing worsening of leaflet tethering.[2]

More recently, attention has been drawn to the preoperative tethering pattern to predict MR recurrence. Nonetheless, the published data are conflicting,[3-5] and it is still unclear whether a specific preoperative leaflet configuration is related to the unfavorable outcomes.

In the present multicenter study, we investigated the relationship between anterior mitral leaflet (AML) tethering characteristics and postoperative MR recurrence.

MATERIALS AND METHODS

Ethical committee approval was waived owing to the retrospective analysis of the study according to national laws regulating observational retrospective studies (Italian law no. 11960, released on July 13, 2004; Dutch WMO law). However, all patients gave their informed consent to access their data for scientific purposes.

The study population consisted of 435 consecutive patients with chronic ischemic MR who survived combined coronary artery bypass grafting and UMRA performed at 3 institutions (University Hospital, Maastricht, The Netherlands; Careggi Hospital, Florence, Italy; and Civic Hospital, Brescia, Italy) from 2001 to 2008. The definition and inclusion and exclusion criteria were as previously reported.[5] The median follow-up was 44.7 months (interquartile range, 25.9–66.4).

All patients underwent complete revascularization. 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 MV area exceeding 2 cm^2 at intraoperative transesophageal echocardiography.

Echocardiographic Studies

Examinations were performed using a commercially available echocardiographic system (IE 33; Philips Medical System, Amsterdam, The Netherlands). Transthoracic echocardiography was performed

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Disclosures: Leen van Garsse, Sandro Gelsomino, Fabiana Lucà, Roberto Lorusso, Carmelo Massimiliano Rao, Pieluigi Stefàno, Jos Maessen have nothing to disclose with regard to commercial support.

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Presented at The American Association for Thoracic Surgery Mitral Conclave, New York, New York, May 5-6, 2011.

Received for publication May 11, 2011; revisions received Sept 15, 2011; accepted for publication Sept 28, 2011; available ahead of print Nov 4, 2011.

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0022-5223/$36.00

doi:10.1016/j.jtcvs.2011.09.061

Abbreviations and Acronyms
AML = anterior mitral leaflet
LV = left ventricular
MR = mitral regurgitation
PML = posterior mitral leaflet
UMRA = undersized mitral ring annuloplasty

before surgery and was repeated annually. All examinations were performed by experienced echocardiographers and stored on a magneto-optical disc. Standard measurements and calculations, quantification of MR, and papillary muscle displacement were performed, as previously reported.[5]

The AML tethering angle α' and the posterior mitral leaflet (PML) angle β' were directly measured with specific software (Philips DICOM Viewer, Philips Medical System). The excursion angles α'_{ex} and β'_{ex} were calculated as the difference between the AML and PML angles in systole and diastole. The anterior/posterior tethering angle ratio α'/β' was a quantitative measurement of tethering. The more this ratio approached 1, the more symmetric was the tethering. Measurements were made off line by 2 cardiologists (F.L. and C.M.R.), who were unaware of the aim of the present study. The Cohen method[6] showed excellent agreement between the intraobserver and interobserver measurements with a concordance of 0.97, 0.98, and 0.96 for α', 0.94, 0.95, and 0.92 for β' and 0.95, 0.98, and 0.94 for coaptation height measured in 20 randomly selected patients for intraobserver 1, intraobserver 2, and interobserver values, respectively. The primary endpoint was the recurrence of MR at the latest echocardiographic follow-up visit. This was defined as insufficiency of 2+ or more in patients with no/trivial MR at discharge.

Patient Classification

The patients were divided by baseline measurements into quintiles of the AML tethering angle α' as follows: group 1, normal/slight AML tethering, α' less than 29.8°; group 2, mild AML tethering, α' of 29.8° or greater but less than 33.4°; group 3, moderate AML tethering, α' of 33.4° or greater but less than 36.9°; group 4, moderate-severe AML tethering, α' of 36.9° or less but less than 40.1°; and group 5, severe AML tethering, α' greater than 40.1°.

The patient characteristics are summarized in Table 1. No difference was found in the baseline demographics and operative variables among the groups. In contrast, significant differences were found in the echocardiographic parameters. The subjects with AML tethering that was moderate-severe or greater had preoperatively larger and more spherical LV ventricles and worse LV function (all, $P < .001$). Furthermore, these patients showed more symmetric tethering ($P = .001$), a lower AML excursion angle ($P = .03$), a more accentuated anterior papillary muscle displacement either in the lateral ($P = .004$) or posterior ($P < .001$) direction, a larger papillary muscle separation ($P = .01$), and a more accentuated anterolateral papillary muscle wall motion score index ($P < .001$).

Statistical Analysis

Continuous data are expressed as the mean ± standard deviation, nonnormal data are presented as the median and interquartile range, and categorical variables as frequencies. The variables were compared across α' categories with analysis of variance, Kruskal-Wallis, and χ^2 tests with Tukey's and Dunn's post hoc tests, as appropriate.

Pearson's correlation analysis was used to test for univariate linear relationships between indexes of tethering and postoperative MR recurrence (regurgitant volume as a continuous variable).

Multivariate logistic regression analysis was performed to assess the effect of preoperative tethering on the recurrence of MR. Forty demographic, clinical, and echocardiographic parameters were chosen on the basis of our previous experience.[5] To enhance the accuracy of the model, the number of variables was reduced using variable clustering. Model fit for logistic regression analysis was assessed with the Hosmer-Lemeshow statistic and predictive accuracy was assessed using the concordance index c.

For presentation purposes, we first analyzed the main effect of preoperative tethering and then investigated the model adjusted for variables recognized as key factors of MR recurrence.[5,7,8] Internal validation of the predictors generated by multivariate logistic regression analysis was performed using bootstrapping techniques, with 1000 cycles and generation of the odds ratios (ORs) and bias-corrected 95% confidence intervals (CIs).

Finally, to assess whether the predictive value of α' was secondary to other factors such as abnormal LV function and geometry, we estimated the effect of α' and β' in subgroups that included the systolic sphericity index (cutoff, 0.7), end-systolic volume (cutoff, 145 mL), myocardial performance index (cutoff, 0.9), wall motion score index (cutoff, 1.5), and coaptation height (cutoff, 11 mm).[5,7,8] For the PML tethering angle, a cutoff of 45° or greater was chosen.[4] The effect of the AML tethering angle in each of the subgroups was estimated using logistic regression analysis and compared with β' of 45 or greater. Next, we tested for interactions between α' and the subgroup variables using a multivariate general linear model.

The Statistical Package for Social Sciences, version 12.0 (SPSS, Chicago, Ill) and StatsDirect, version 2.5.7 (StatsDirect, Cheshire, UK) were used for these calculations.

RESULTS

Recurrent MR

At follow-up, 99 patients (22.7%) showed recurrent MR. It developed in 39.4% of patients with severe (n = 39), 28.3% with moderate-severe (n = 28), 15.1% with moderate (n = 15), 11.1% with mild (n = 11), and 6.1% with normal/slight (n = 6) AML tethering. The tenting area was reduced preoperatively in groups 1 to 3 (2.5 cm^2, 2.7 cm^2, and 2.7 cm^2, respectively; $P < .001$) but did not change significantly in groups 4 and 5 (3.8 cm^2 and 3.7 cm^2, respectively; $P < .001$ vs groups 1–3). The coaptation length was less than 8 mm in all patients in groups 4 and 5 (3.9 mm and 3.6 mm, respectively), and it was lower than in groups 1 to 3 (8.4 mm, 8.4 mm, and 8.6 mm, respectively; $P < .001$ vs groups 1–3). At follow-up, 90 (90.9%) of 99 patients with recurrent MR had asymmetric tethering with an eccentric jet without difference among the groups ($P = .87$ and $P = .9$, respectively).

Associations With Outcome

For all subjects, a strong correlation was found between the anterior mitral leaflet angle and recurrent MR ($r = 0.83$, $P < .001$). This correlation was stronger in patients with severe AML tethering ($r = 0.95$, $P < .001$) than in those with moderate-severe ($r = 0.56$, $P = .008$), moderate ($r = 0.55$, $P = .01$), mild ($r = 0.50$, $P = .03$), or slight ($r = 0.31$, $P = .04$) AML tethering. In contrast, the correlation between the PML angle and MR recurrence was weak ($r = 0.12$, $P = .05$). Among the parameters of leaflet tethering, the correlation was significant between α'/β' ($r = 0.88$, $P < .001$). Furthermore, a good correlation