Original Research

CARDIAC IMAGE UPDATED

Vol. 1, No. 1, January-March 2019

Radial deformation and left ventricle rotation of the base are mechanisms associated with the severity of primary mitral regurgitation

La deformación radial y la rotación de la base del ventrículo izquierdo son mecanismos asociados con la gravedad de la regurgitación mitral primaria

Nydia Ávila Vanzzini,* Juan Francisco Fritche-Salazar,* Nestor Alejandro Parra Ordoñez,* Héctor Herrera Bello**

* Instituto Nacional de Cardiología «Ignacio Chávez».
** Fundación Clínica Médica Sur.

ABSTRACT. Introduction: The rotational mechanics of the left ventricle (LV) are part of the function of the mitral annulus; the loss of this mechanism has been associated with the severity of mitral regurgitation (MR). Our objective was to evaluate whether the rotation of the LV base is a mechanism associated with the severity of MR. **Methods:** A cross-sectional analytical study was designed. Patients older than 18 years old with non-ischemic MR were included. A healthy control group was analized. **Results:** Ninety-one participants were included, 57 cases and 34 controls. The patients with MR had worse ventricular strain (longitudinal, radial and circumferential). The case group were divided by severity of regurgitation; longitudinal strain had a progressive decrease from mild to severe MR (-19% [95%CI -22%-15%] and -14% [95%CI -17%-6%]) respectively (p<0.033). Twist in patients with mild MR was 16º (13.6-19.4), which decreases to 10.8º (7.3-17.3) in severe MR (p<0.034), torsion shows a similar pattern with a value of 2.05º/cm, in the mild MR, and that decreases to 1.1º/cm in severe MR (p<0.038). Multivariate analysis shown that the independents mechanisms associated with severity of MR were: radial strain (OR:1.08, 95%CI:1.03-1.13, p<0.006), and basal rotation [OR:1.14 95% CI 1.07-1.26, p<0.02]. **Conclusion:** In MR of non-ischemic etiology, poor rotation of the base and poor radial strain were associated with MR severity.

Key words: Mitral regurgitation, ventricular rotational mechanics, basal rotation.

RESUMEN. Introducción: *La mecánica de rotación del ventrículo izquierdo (VI) es parte de la función del anillo mitral; la pérdida de este mecanismo se ha asociado con la gravedad de la regurgitación mitral (RM). Nuestro objetivo fue evaluar si la rotación de la base de BT es un mecanismo asociado con la severidad de la RM.* ***Métodos:*** *Se diseñó un estudio analítico transversal. Se incluyeron los pacientes mayores de 18 años con RMN no isquémica. Se analizó un grupo de control sano.* ***Resultados:*** *Se incluyeron 91 participantes, 57 casos y 34 controles. Los pacientes con RM tuvieron peor tensión ventricular (longitudinal, radial y circunferencial). El grupo de casos se dividió por la gravedad de la regurgitación; la deformación longitudinal tuvo una disminución progresiva de leve a severa RM (-19.1% [IC 95% -22-15.7%] a -14% [IC 95% -17.8-6.7%]) respectivamente (p<0.033). La torsión en pacientes con RM leve fue de 16º (13.6-19.4), que disminuye a 10.8º (7.3-17.3) en la RM grave (p<0.034), la torsión muestra un patrón similar con un valor de 2.05º/cm, en la RM leve, y que disminuye a 1.1º/cm en la RM grave (p<0.038). El análisis multivariado mostró que los mecanismos independientes asociados con la gravedad de la RM fueron: deformación radial (OR: 1.08; IC 95%: 1.03 a 1.13; p<0.006) y rotación basal (OR: 1.14; IC 95%: 1.07 a 1.26; p<0.02).* ***Conclusión:*** *En la RM de etiología no isquémica, la mala rotación de la base y la mala deformación radial se asociaron con la gravedad de la RM.*

Palabras clave: *Regurgitación mitral, mecánica de rotación ventricular, rotación basal.*

Corresponding author:
Nydia Ávila-Vanzzini
Departamento de consulta externa.
Instituto Nacional de Cardiología «Ignacio Chávez».
Juan Badiano Núm. 1, Col. Sección XVI, Tlalpan, 14080, Ciudad de México, México.
Teléfono: +52 (55) 55-73-29-11
Fax: +52 (55) 55730994
E-mail: vazzny74@yahoo.com

INTRODUCTION

Mitral regurgitation (MR) generates a chronic volume overload, leading to irreversible left ventricular (LV) dysfunction.[1] Several coexisting pathophysiologic mechanisms are independently involved in MR pathogenesis, including LV systolic dysfunction, LV local and global remodeling, LV dyssynchrony, annular shape, and organic alterations.[2,3] In ischemic MR the restricted sphincter motion of the mitral annulus (MA) and the impaired basal rotation, consequence of an inferior-posterior myocardial infarction, have been associated with increased of MR severity.[4] Advances in cardiac imaging techniques have provided new insights into LV mechanics.[5] The rotation obtained by 2-dimensional speckle tracking echocardiography, hold promise to be a more reliable index of «myocardial performance». In chronic MR correlations between disease severity and torsional parameters suggest a potential role of these variables in assessing early signs of ventricular dysfunction;[6] however, it has not been evaluated in different etiologies of MR and the mechanism by which the antero-posterior annular function is loss is not fully understood. In the present study, we sought to investigate whether basal rotational mechanical failure is associated with increased severity of MR and to provide a hypothesis for the pathophysiologic mechanism by which the annular function is lost.

METHODS

A cross-sectional study was designed; patients older than 18 years attending to echocardiographic evaluation from March to August 2017 with the diagnosis of MR were consecutively included. We evaluated 186 patients with functional non-ischemic or organic MR. Were excluded patients with clinical and echocardiographic evidence of other cardiac and/or heart valve disease (45), previous cardiac surgery (6), previous treatment with chemotherapy (2), acute o chronic myocardial infarction (28), atrial fibrillation (9), inflammatory diseases (4), left bundle branch block (5), and technically inadequate two-dimensional echocardiographic images for speckle-tracking echocardiographic analysis (14). About mechanism of MR were excluded patients with flail (4) and ischemic mitral regurgitation (12). A healthy young control group or 34 people was analyzed. All the patients underwent preliminary cardiologic examinations with comprehensive clinical data collection, including cardiovascular risk factors, electrocardiogram and transthoracic echocardiogram. The study was approved by the local research and ethics committee and follows the Helsinki guidelines.

Two-dimensional echocardiography. Each subject underwent standard transthoracic echocardiogram using Vivid 9 XD clear echocardiography equipment (GE Vingmed Ultrasound AS, Horten, Norway) according to the American Society of Echocardiography guidelines.[7] The parameters of LV global remodeling, including LV end-diastolic volume (EDV), end-systolic volume (ESV) and biplane Simpson's ejection fraction, were measured. LV volumes were indexed.

Global LV strain and rotational mechanics. Ventricular mechanics were performed according to actual recommendations.[8] For offline analysis of strain and rotation, LV short-axis views acquired at the basal, mid and apical levels, and standard LV apical four-chambers, three chamber and two-chamber views were recorded with a mean frame rate or ≥70 frames/sec. Two-dimensional strain and rotation data were analyzed by frame-to-frame tracking of the grayscale patterns using dedicated software of Echopac.

Evaluation of mitral regurgitation. In the case of a single jet, the contract vein (CV) was measured on the perpendicular axis to the regurgitant jet; a CV <0.3 cm was equivalent to mild insufficiency, a CV ≥0.7 cm was equal to severe insufficiency, the intermediate points were evaluated with quantitative methods such as the flow convergence method (PISA). If two or more jets were found, the severity assessment was made using the Doppler continuity method, in accordance with the recommendations for the assessment of valvular regurgitation.[9] Both the PISA method and the continuity method considered a regurgitant orifice area (AORE) ≥0.40cm^2 and regurgitant volume (RVol) ≥60mL as severe; AORE of 0.20-

0.39cm^2 and RVol of 30-59mL was considered moderate, and AORE <20cm^2 and <30mL of RVol, was considered mild.[9]

Statistic analysis

Normality of the continuous variables was sought with the Shapiro Wilk test. The parametric variables are expressed as mean and standard deviation and their comparison was made with Student's t-test; the non-parametric variables are expressed in median and interquartile range (25-75); their comparison was made with the Wilcoxon sum-rank test. The comparison of more than two groups of continuous variables was performed with the one-way analysis of variance (ANOVA) or the Kruskal Wallis test as appropriate. The categorical variables are expressed as a percentage and their comparison between groups was performed with the χ^2 test. A value of $p<0.05$ was considered as statistical significant.

RESULTS

A total of 91 participants were included, 57 were cases and 34 controls. Differences in age, height, systemic arterial hypertension (SAH) and dyslipidemia were observed between cases and controls; in the echocardiographic findings there was a significant difference in: left ventricular ejection fraction (LVEF), left atrium volume (LAV), systolic mitral annulus dimension, fractional shortening of the mitral annulus, tenting area and depth of coaptation. In the analysis of ventricular mechanics, the case group showed a significant decrease in the overall longitudinal, radial and circumferential deformation, as well as a decrease in basal rotation, twist and torsion in relation to the control group *(Table 1)*.

Analysis by subgroups according to the severity of mitral regurgitation. Differences were found in EDV, ESV and LAV, they shown a progressive increased in relation to the severity of MR; p<0.0027; p<0.0085 and p<0.001; mild, moderate and severe respectively). The same behavior was observed in the anterior-posterior diameter of the mitral annulus, which was larger the more severe the MR was (p<0.001; p<0.0001 diastolic and systolic annulus respectively). The shortening fraction of mitral annulus was clearly compromised in severe MR, p<0.0008. A progressive decrease in the LVEF was observed p<0.013 *(Table 2)*. Tenting area and depth of coaptation were greater among the more severe was the regurgitation p<0.0009; p<0.045 respectively. The longitudinal global strain showed a significant progressive decrease from mild MR (-19.1% [-22%-15.7%], moderate MR -18.1% [-21%-14.7%] and severe MR -14% [-17.8%-6.7%]) (p<0.033) (the rest of the deformation vectors are shown in *Table 2)*. The basal rotation was statistically different between the mild and severe MR groups; p<0.043. The twist in mild MR was 16º (13.6-19.4), this decreased to 10.8º (7.3-17.3) in severe MR; p<0.034; the torsion shows a similar pattern with a value of 2.05º/cm (1.6-2.4) in mild MR, and 1.1º/cm (0.8-2.1) in severe MR; p<0.038. *(Figure 1 and Table 2)*. A multivariate analysis (logistic regression) was performed to search variables associated with moderate or severe MR; global radial strain (GRS) [OR 1.08, 95%CI 1.03-1.13, p<0.006] and basal rotation [OR: 1.14, 95%CI 1.07-1.26, p<0.02] were independently associated with a higher MR severity *(Table 3)*.

Interobserver variability. Intraclass correlation coefficients were performed for longitudinal, circumferential, radial and rotational profiles, according to what was reported in previous studies, a variability of 5 and 3% was obtained for longitudinal and circumferential deformation respectively, the ventricular mechanics parameters had the best reproducibility *(Table 4)*.

DISCUSSION

This study shows that the decrease in rotation of the base of the LV and the decrease in the radial deformation are associated with a greater severity of MR in patients with MR of degenerative and non-ischemic functional etiology. This phenomenon had already been observed previously in patients with MR of ischemic etiology; Zito et al[4] reported the impaired basal rotational mechanics occurring after an inferior-posterior myocardial infarction is associated with increased MR. In another study of patients with different MR etiology

Table 1: Clinical and echocardiographic findings in both groups.

	Control group n = 34	MR Group n = 57	p
Age (years)	26 (21-33)	54 (47-62)	0.00001
Female (%)	19 (55.8)	32 (56.1)	0.981
Height (cm)	167 ± 10	170 ± 11	0.009
Weight (kg)	67 (56-78)	68 (59-76)	0.457
SAH (%)	0	21 (36.8)	0.0001
DL (%)	0	14 (24.5)	0.002
Echocardiographic findings			
EDV (mL/m^2)	50 (42-60)	55 (49-60)	0.067
ESV (mL/m^2)	21 (16-25)	23 (18-39)	0.058
LAV (mL/m^2)	15 (11-19)	23 (19-35)	0.0001
LVEF (%)	60.5 (60-65)	55 (49-60)	0.0001
Measurement of the mitral valve			
MAD (mm)	31 ± 3.8	33 ± 5.3	0.081
MAS (mm)	24 (20-28)	28 (23-33)	0.024
SFMA (%)	21 (15-28)	12 (6-21)	0.018
Tenting area (cm^2)	0.9 (0.7-1.4)	1.9 (1.6-2.5)	0.0001
Depth of coaptation (mm)	0.7 (0.6-0.9)	1 (0.7-1.2)	0.0015
Ventricular mechanics			
GLS (%)	-22 (-23 to -20.5)	-17.4 (-21.8 to -12.7)	0.0001
GCS (%)	-25 (-29 to -20)	-16.3 (-21 to -13)	0.0001
GRS (%)	42 (33-47)	22 (15.9-28)	0.0001
Basal rotation (º)	-6.7 (-7.3 to -5)	-4.2 (-6.7 to -3)	0.041
Apical rotation (º)	11 (9-11)	10 (6-13)	0.05
Twist (º)	17 (15-18)	14 (10-18)	0.007
Torsion (º/cm)	2.0 (1.8-2.2)	1.8 (1.3-2.3)	0.047

SAH = systemic arterial hypertension; DL = dyslipidemia; EDV = end diastolic volume; ESV = end systolic volume; LAV = left atrial volume; LVEF = left ventricular ejection fraction; MAD = diameter of mitral annulus in diastole; MAS = diameter mitral annulus in systole; SFMA = shortening fraction of mitral annulus; GLS = global longitudinal strain, GCS = global circumferential strain; GRS = global radial strain.

(mitral valve prolapse), Zito et al[10] found that the basal rotation increased progressively in proportion to the severity of the MR, and the torsion reached the maximum peak in patients with moderate MR and decreased in those with severe MR; these results are different from our study; while Zito el al[10] were looking for predictors of myocardial function, we seek to associate the mechanics of rotation of the base of LV to the degree of MR, Zito included only patients with LVEF ≥60% and the decrease in LVEF was not an exclusion criterion for us; thus our patients had more altered rotation patterns.

Under normal conditions, the twisting motion of the heart (LV twist is the preferred nomenclature for the measurement defined as the difference in the rotation of the apex relative to that of the base of the heart), arises from transmural differences in the local myofiber orientation, which is thought to minimize transmural stress gradients.[11] On the other hand, basal rotation shortens the distance between the MV and the head of papillary muscles, this mechanism might contribute to MV leaflet closure and counterbalancing the tethering forces. In relation to the mitral

Table 2: Analysis by subgroups according to the severity of mitral regurgitation.

	Mild MR n = 26	Moderate MR n = 12	Severe MR n = 19	p
Age (years)	51 (44-62)	54 (46-60)	55 (47-62)	0.824
Female (%)	15 (58)	9 (75)	8 (42)	0.089
Height (cm)	162 ± 12	159 ± 10	161 ± 9	0.701
SAH (%)	8 (31)	5 (42)	8 (42)	0.684
DL (%)	6 (23)	3 (25)	5 (26)	0.969
Echocardiographic findings				
EDV (mL/m^2)	44 (44-58)	57 (44-87)	79 (51-97)*	0.0027
ESV (mL/m^2)	19 (13-31)	25 (16-39)	32 (23-62)*	0.0085
LAV (mL/m^2)	40 (32-50)	61 (51-68)‡	79 (74-128)*	0.001
LVEF (%)	60 (55-61)	58 (53-63)	50 (26-55)*	0.013
Measurement of the mitral valve				
MAD (mm)	30 ± 3.8	31.6 ± 4.6	36.4 ± 5.1*	0.001
MAS (mm)	25 ± 4	26 ± 6	34 ± 5*	0.0001
SFMA (%)	17 (7-24)	17 (11-29)	6 (2-12)*	0.0008
Tenting area (cm^2)	1.6 (1.1-2.1)	1.8 (1.4-2.1)	2.5 (2.3-3.1)*	0.0009
Depth coaptation (mm)	0.9 (0.6-1)	0.95 (0.8-1.1)	1.1 (0.9-1.4)*	0.045
Ventricular mechanics				
GLS (%)	-19 (-22 to -15)	-18 (-21 to -14)	-14 (-17 to -6)*	0.033
GCS (%)	-17 (-21 to -15)	-16 (-20 to -13)	-15 (-17 to -8)	0.141
GRS (%)	25.5 (19-31)	17 (13.5-24.5)	19 (14-27)	0.099
Basal rotation (º)	-6 (-8.2 to -3.7)	-4.5 (-6 to -2.4)	-3.4 (-6 to-1.9)*	0.043
Apical rotation (º)	10.8 (7.3-13)	9.5 (7.6-13)	6.5 (4.2-14.5)	0.304
Twist (º)	16 (13.6-19.4)	14.5 (11.4-17)	10.8 (7.3-17.3)*	0.034
Torsion (º/cm)	2.05 (1.6-2.4)	1.65 (1.35-2.2)	1.1 (0.8-2.1)*	0.038

Abbreviations in previous table.
*Differences between mild and severe MR. ‡Differences between mild and moderate MR.

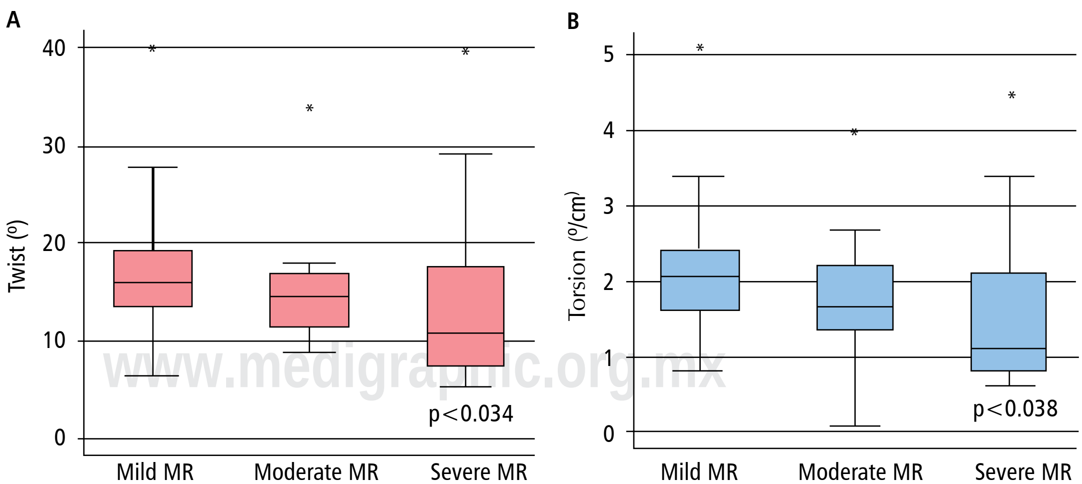

Figure 1: Evaluation of twist and torsion in different degrees of severity of mitral regurgitation.
Analysis of twist and torsion by speckle tracking 2D. **A.** Show that the twist is smaller as the severity of the mitral regurgitation increases. **B.** The same behavior is observed in the analysis of the torsion, show statistic differences.

Table 3: Multivariate analysis, association with moderate to severe mitral regurgitation.

Variable	OR	z	p (> Z)	95% CI
GLS	1.18	1.95	0.052	0.99-1.41
GCS	1.11	1.43	0.152	0.96-1.29
GRS	1.08	2.74	0.006	1.03-1.13
AR	0.85	-1.4	0.163	0.68-1.06
BR	1.14	2.96	0.02	1.07-1.26
Twist	1.11	0.62	0.53	0.79-1.55
Torsion	1.40	0.36	0.72	0.21-9.10

AR = apical rotation; BR = basal rotation. Rest of abbreviations in Table 1.

Table 4: Interobserver variability.

	Intraclass coefficient	p
GLS	0.955	0.0001
GRS	0.796	0.0150
GCS	0.975	0.0001
Basal rotation	0.892	0.0010
Apical rotation	0.738	0.0290
Twist	0.778	0.0180
Torsion	0.821	0.0090

annulus, its mechanism is useful to maintain MV competence; contraction of the sphincter of the posterior annulus caused by the shortening of the basal helical fibers of the ventricle, creates a competent superimposed coaptation.

Primary MR is characterized by an incomplete closure of the mitral valve, which permits the flow of blood across the mitral valve during systole (decreased afterload) and leads to increased EDV (increased preload). In chronic MR with preserved myocardial structure (without loss of the helical architecture of the fibers) the increase of the preload increases the rotation of the base and apex of the LV[12] as was described in the Zito Study;[10] but if it already exists increased LV sphericity and loss of the oblique architecture of the apical and basal fibers, the rotational mechanisms of the ventricle become affected, which in turn leads to a deficient function of sphincter of the mitral annulus and this is what can explain a possible added mechanism in the severity of the MR. Hence LV torsional parameters corelate with the degree of LV remodeling and the severity of MR.[13]

CONCLUSION

In patients with MR of degenerative and non-ischemic etiology, poor rotation of the base and poor radial strain were associated as independently variables with MR severity.

Limitations of study

Our results have to be considered within the context of some limitations. The study population was small and came from a single tertiary center. It is a cross-sectional study focused basically on the evaluation of the rotational mechanics and MR, so the LVEF was not taken into account as a selection criteria of patients.

REFERENCES

1. Avierinos JF, Gersh BJ, Melton LJ 3rd et al. Natural history of asymptomatic mitral valve prolapse in the community. Circulation. 2002; 106: 1355-1361.
2. Agricola E, D'Amato R, Stella S et al. Effects of mild ischemic mitral regurgitation on ventricular remodeling and its contribution to congestive heart failure. J Am Soc Echocardiogr. 2011; 24: 1376-1382.
3. Agricola E, Oppizzi M, Pisani M, Meris A, Maisano F, Margonato A. Ischemic mitral regurgitation: mechanisms and echocardiographic classification. Eur J Echocardiogr. 2008; 9 (2): 207-221.
4. Zito C, Cusma-Piccione M, Oreto L et al. In patients with post-infarction left ventricular dysfunction, how

does impaired basal rotation affect chronic ischemic mitral regurgitation? J Am Soc Echocardiogr. 2013; 26: 1118-1129.
5. Sengupta PP, Tajik AJ, Chandrasekaran K, Khandheria BK. Twist mechanics of the left ventricle: principles and application. JACC Cardiovascular Imaging. 2008; 1: 366-376.
6. Borg AN, Harrison JL, Argyle RA, Ray SG. Left ventricular torsion in primary chronic mitral regurgitation. Heart (British Cardiac Society). 2008; 94: 597-603.
7. Lang RM, Badano LP, Mor-Avi V et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2015; 16 (3): 233-270.
8. Mor-Avi V, Lang RM, Badano LP et al. Current and evolving echocardiographic techniques for the quantitative evaluation of cardiac mechanics: ASE/EAE consensus statement on methodology and indications endorsed by the Japanese Society of Echocardiography. J Am Soc Echocardiogr. 2011; 24 (3): 277-313.
9. Lancellotti P, Moura L, Pierard LA et al. European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 2: mitral and tricuspid regurgitation (native valve disease). Eur J Echocardiogr. 2010; 11 (4): 307-332.
10. Zito C, Carerj S, Todaro MC et al. Myocardial deformation and rotational profiles in mitral valve prolapse. Am J Cardiol. 2013; 112 (7): 984-990.
11. Bovendeerd PH, Arts T, Huyghe JM, van Campen DH, Reneman RS. Dependence of local left ventricular wall mechanics on myocardial fiber orientation: a model study. J Biomech. 1992; 25 (10): 1129-1140.
12. Omar AM, Vallabhajosyula S, Sengupta PP. Left ventricular twist and torsion: research observations and clinical applications. Circ Cardiovasc Imaging. 2015; 8 (6). pii: e003029.
13. Reyhan M, Wang Z, Li M et al. Left ventricular twist and shear in patients with primary mitral regurgitation. J Magn Reson Imaging. 2014; 42 (2): 400-406.