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Mitral Valve Remodeling after Acute Myocardial Infarction – a Longitudinal Three-Dimensional Echocardiography Study

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Abstract

Background: Recent data suggest that the mechanisms contributing to ischaemic mitral regurgitation (IMR) in the setting of acute myocardial infarction (MI) are different compared to chronic IMR. However, little is known about the dynamic changes over time of mitral valve (MV) geometry after acute MI. **Methods and results:** Comprehensive three-dimensional (3D) assessment of the MV geometry was performed in 30 patients in the first 7 days after a first ST elevation myocardial infarction (STEMI), and after 4 years of follow-up. The MV annulus diameters and area remained unchanged over time, however the MA became progressively flatter (mean difference of annular height 0.19±0.33 cm, $p<0.05$), independently of the presence or severity of IMR. The posterior leaflet length and area got smaller over time (1.53±0.51 cm vs 1.27±0.33 cm; $p<0.05$ and 5.65±1.58 cm^2 vs 4.88±1.65 cm^2; $p<0.05$, respectively). The tenting height and area were smaller at follow-up (9.06±2.6 mm vs 7.84±2.61 mm, $p<0.05$; and 1.88±0.6 cm^2 vs 1.57±0.5 cm^2; $p<0.05$, respectively). A larger tenting at follow-up correlated with 3D left atrial (LA) volumes, but not with LV volumes and ejection fraction. **Conclusions:** MV geometry changes over time even in patients with non-severe IMR. The MV healing process consists in annulus flattening associated with improved tenting.

Keywords: ischaemic mitral regurgitation, mitral valve geometry, acute myocardial infarction, three-dimensional echocardiography.

Rezumat

Context: Cercetările recente au arătat că mecanismele care stau la baza regurgitării mitrale ischemice (RMI) în contextul infarctului miocardic (IM) acut sunt diferite față de mecanismele RMI cronice. Totuși, există puține informații referitoare la modificările în timp ale geometriei valvei mitrale după un IM acut. **Metode și rezultate:** Geometria valvei mitrale a fost analizată prin ecocardiografie tridimensională (3D) la 30 de pacienți în primele 7 zile după infarct cu supradenivelare de segment ST (STEMI), și după 4 ani de urmărire. Diametrele și aria inelului mitral nu s-au modificat în timp, totuși inelul mitral s-a aplatizat progresiv (diferența medie a înălțimii inelului 0,19±0,33 cm, $p<0,05$), independent de prezența sau severitatea RMI. Lungimea și aria foiței mitrale posterioare a devenit mai mică în timp (1,53±0,51 cm vs 1,27±0,33 cm; $p<0,05$ și respectiv 5,65±1,58 cm^2 vs 4,88±1,65 cm^2; $p<0,05$). Înălțimea și aria de tenting au devenit mai mici în timp (9,06±2,6 mm vs 7,84±2,61 mm, $p<0,05$; și respectiv 1,88±0,6 cm^2 vs 1,57±0,5 cm^2; $p<0,05$). Parametrii de tenting mai mari la vizita finală s-au corelat cu volumele 3D ale atriului stâng (AS) dar nu cu volumele și fracția de ejecție a ventriculului stâng. **Concluzii:** Geometria valvei mitrale se modifică

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în timp chiar și la pacienții cu RMI non-severă. Procesul de vindecare al valvei mitrale constă în aplatizarea inelului mitral asociată cu ameliorarea parametrilor de tenting.

Cuvinte cheie: regurgitare mitrală ischemică, geometria valvei mitrale, infarct miocardic acut, ecocardiografie tridimensională.

INTRODUCTION

Ischaemic mitral regurgitation (IMR) is frequently encountered in ischaemic heart disease (IHD) and it is associated with worse prognosis in this population of patients[1]. IMR is characterized by normal morphology of the mitral valve (MV) apparatus, but apical displacement of papillary muscles (PM) and tethered mitral leaflets in the context of an enlarged and dysfunctional left ventricle (LV)[2]. The majority of studies on IMR has been focused on patients with chronic IHD and less attention was payed to acute IMR. However, recently it was demonstrated that the mechanism of IMR in the setting of acute myocardial infarction (MI) is different from the mechanism of chronic IMR[3,4].

Recent studies comparing cohorts of patients with significant acute versus chronic IMR have demonstrated that in chronic IMR the MV annular surface is larger, the annular height is smaller (the annulus is flatter) and the leaflets surface is larger, with a larger tenting volume[3,4]. However, few little is known about the MV geometrical changes over time in the same cohort of patients. Furthermore, there is little data concerning the MV geometrical changes over time in patients without severe IMR. The process of „healing" of the MV after acute MI has not been described.

Three-dimensional (3D) echocardiography permits the unique opportunity to assess the intimate geometrical relationships between MV apparatus components.

In this study we sought to describe the MV geometrical alterations over time in a cohort of patients with acute STEMI without or with non-severe IMR.

METHODS

We prospectively included patients with a first acute STEMI who were treated by primary percutaneous intervention (PCI). Patients with prior MI, heart failure, cardiomyopathy/apical-ballooning, or coronary bypass surgery were excluded as well as patients with organic MV disease such as myxomatous degeneration or thickening due to rheumatic heart disease.

Comprehensive two-dimensional (2D) and 3D transthoracic echocardiography was performed in 30 patients in the first 7 days after a first STEMI, and after 4 years of follow-up.

The echocardiographic examinations were performed using VividV9 (GE Vingmed Ultrasound AS, Horten, Norway). Two-dimensional (2D) and 3D full-volumetric images were obtained from apical view.

Image analysis was performed offline with GE EchoPAC work station software version 113.1.1 (GE Vingmed Ultrasound AS, Horten, Norway) after image acquisistion. 3D LV and LA volumes, ejection fraction (EF), and stroke volume (SV) were measured using EchoPAC BT13, 4D Auto-LVQ software, (GE Vingmed-Ultrasound, Horten, Norway).

The severity of IMR was semi-quantified using color flow Doppler, to which further quantitative parameters were added in cases of moderate IMR.

The MV geometry was assessed using 4D Auto MVQ software, GE Vingmed Ultrasound AS, Horten, Norway).

First, the mid-systolic frame was selected taking into account the ECG trace as well as the MV opening and closure. Then the image was aligned so that the LA was shown above the MV (Figure 1A). The next step consisted in placing 4 annular points representing the medial, lateral, anterior, and posterior mitral annulus landmarks. These points were identified on 2 different longitudinal and perpendicular planes. Then, an additional point was placed in the center of the aortic valve (Figure 1B), a point at the MV coaptation and one point at the apical point of the aortic annulus (Figure 1C). These served as reference points for the identification of different MV annular regions. Finally, the automated tracking workflow delivered a 3D rendered volume of the MV, allowing a comprehensive visualization of any structural deformation in the saddle shaped, nonplanar configuration of MV annulus and any abnormality in leaflet morphology (Figure 1E)[5,6].

The automatically generated contours were corrected if necessary, in order to accurately follow the realistic contours of MV annulus and leaflets (Figure 1D).

The software returned several MV annulus geometrical parameters: antero-posterior (AP) diameter of the mitral annulus; anterolateral to posteromedial (AL-PM) diameter of the mitral annulus; MV annu-

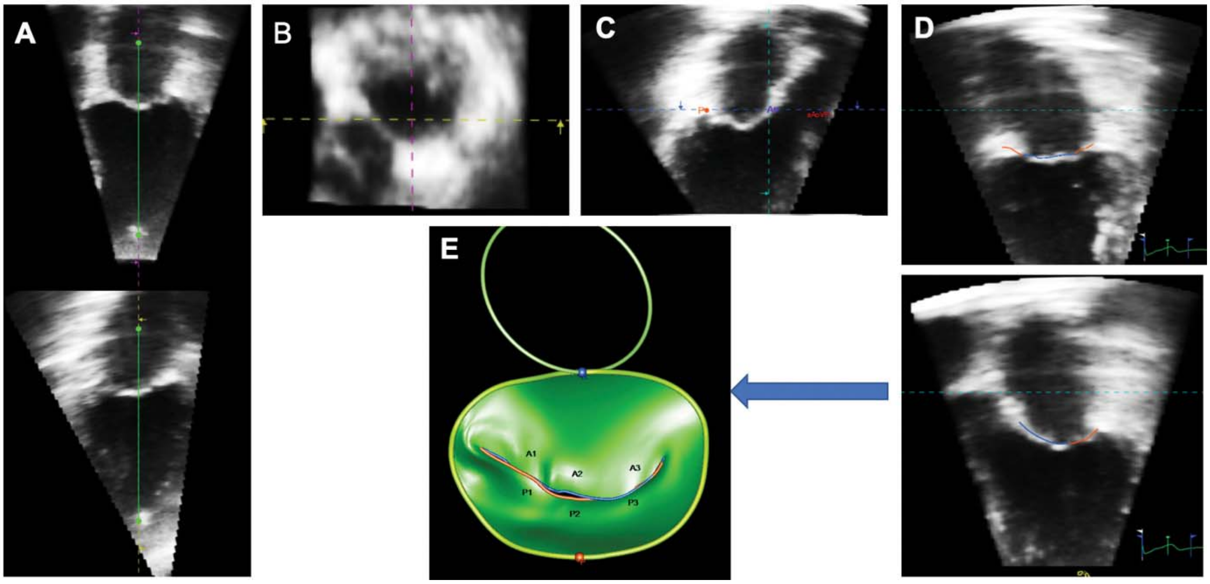

Figure 1. Mitral valve (MV) assessment workflow. **A.** The image is aligned so that the left atrium is shown above the MV. Then 4 points are placed on the medial, lateral, anterior, and posterior aspects of the mitral annulus. **B.** An additional point is placed in the center of the aortic valve. **C.** One point is placed at the apical point of the aortic annulus. These served as reference points for the identification of different MV annular regions. **D.** The automatically generated contours may be corrected if necessary, in order to accurately follow the realistic contours of MV annulus and leaflets. **E.** Finally, the automated tracking workflow delivered a 3D rendered volume of the MV, allowing a comprehensive visualization of any structural deformation in the saddle shaped, nonplanar configuration of MV annulus and any abnormality in leaflet morphology.

lus circumference, height, 2D and 3D area; sphericity index (the ratio between AP and AL-PM diameter); nonplanar angle, subtended by 2 lines connecting the middle point of the commissural diameter, respectively, with the anterior and the posterior annulus highest points, a measure of the saddle shape of the mitral annulus. Furthermore, several parameters describing the mitral leaflets morphology were returned: tenting volume, tenting area, tenting height, commissural diameter, anterior leaflet area, posterior leaflet area, anterior leaflet length, posterior leaflet length and posterior leaflet angle.

STATISTICAL ANALYSIS

Results were expressed as mean ± standard deviation for continuous variables and percentage for categorical variables. Differences between early and late follow-up echocardiographic parameters were analyzed with the paired sample *t*-tests. A 2-sided P value <0.05 was considered to indicate statistical significance. Pearson correlation coefficient was used to assess the relationship between MV geometrical parameters and LV and LA 3D volumes and function. All analyses were performed using IBM SPSS Statistics (version 22; IBM Corporation, Somers, NY).

RESULTS

Thirty patients (22% females, mean age of 63,7 years) were analyzed early after acute MI and at follow up (after 4 years). MI had an anterior location in 15 patients (50%). The 3D echocardiography was performed in the 7th day after acute STEMI and after 4 years follow-up. At the baseline assessment, the mean 3D LV end-diastolic, end-systolic and ejection fraction were 97.12 ml, 52.52 ml and 46.48%. After 4 years, the 3D LV end-diastolic, end-systolic and ejection fraction were 107.76 ml, 52.96 ml and 51.69%.

Of the 30 patients, 12 had no MR, 10 had mild MR and 4 had moderate MR. The degree of IMR did not aggravate overtime in any of the 30 patients.

MV GEOMETRY IN THE SETTING OF ACUTE MI

Early after acute MI, the mitral annulus had an average circumference of 11.35±1.1 cm, a height of 0.88±0.33 cm and a sphericity index of 1 (AP diameter/ AL-PM diameter = 3.13±0.34 cm / 3.65±0.6 cm) (Table 1). The 3D measured annulus area was significantly larger than the 2D measured one (9.59±1.84 cm^2 vs 9.29±1.76 cm^2, p= 0.006).

The anterior leaflet length was smaller than the length of posterior leaflet (2.18±0.39 cm vs 1.53±0.51 cm, $p<0.05$), however the anterior and posterior leaflet areas were similar (5.82±1.13 cm^2 vs 5.65±1.58 cm^2, p= 0.699). The average tenting height, area and volume were 9.06±2.6 mm, 1.88±0.6 cm^2 and 3.12±1.4 cm^3, respectively.

There were no significant difference regarding MV geometry parameters in patients with compared to those without IMR. Similarly, the location of MI (anterior vs non-anterior) had no impact on the measured MV geometry parameters.

MV GEOMETRY CHANGES LATE AFTER MI

On late follow-up there was no significant difference regarding the average annulus AP diameter, AL-PM diameter or circumference, however the annulus sphericity index was smaller (1 vs 0.84±0.09, $p<0.05$) (Table 1). Similarly, the 2D and 3D measured annulus areas were unchanged, however the annulus height at follow-up was smaller than in the setting of acute MI (0.69±0.16 cm vs 0.88±0.33 cm, $p<0.05$).

The anterior leaflet length was larger at follow-up than in the acute setting (2.4±0.32 vs 2.18±0.39, $p<0.05$), however the anterior leaflet area was similar between the two examinations (p=0.273). On contrary, the posterior leaflet length and area were smaller at follow-up than in the acute setting (1.27±0.33 cm vs 1.53±0.51 cm, $p<0.05$ and 4.88±1.65 cm^2 vs 5.65±1.58 cm^2, $p<0.05$, respectively). The tenting height and area were smaller at follow-up (9.06±2.6 mm vs 7.84±2.61 mm, $p<0.05$, and 1.88±0.6 cm^2 vs 1.57±0.5 cm^2, $p<0.05$, respectively). However, the tenting volume were similar between the two examinations (p=0.104). The posterior leaflet length and area correlated with the tenting area (r 0.844; $p<0.001$ and r 0.810; $p<0.001$).

MV GEOMETRY IN RELATION TO THE LEFT VENTRICLE AND ATRIUM

For this analysis we chose only the MV geometry parameters that changed over time. A larger tenting hei-

Table 1. Mitral valve geometrical parameters early and late after myocardial infarction

Geometrical parameter	Early	Late	Mean difference	p
Annulus				
AP diameter (cm)	3.13±0.34	3.06±0.44	0.06±0.44	0.58
AL-PM diameter (cm)	3.65±0.6	3.68±0.4	0.03±0.59	0.813
Annulus circumference (cm)	11.35±1.1	11.31±1.2	0.04±0.93	0.859
Sphericity index	1	0.84±0.09	0.16±0.09	<0.05
Non-planar angle (°)	146.82±11	154.71±12	7.88±14.44	<0.05
2D annulus area (cm^2)	9.29±1.76	9.22±2	0.07±1.48	0.841
3D annulus area (cm^2)	9.59±1.84	9.5±2	0.09±1.58	0.814
Annulus height (cm)	0.88±0.33	0.69±0.16	0.19±0.33	<0.05
Leaflets				
Tenting volume (cm^3)	3.12±1.4	2.7±1.1	0.4±0.96	0.104
Tenting area (cm^2)	1.88±0.6	1.57±0.5	0.3±0.47	<0.05
Tenting height (mm)	9.06±2.6	7.84±2.61	1.21±1.97	<0.05
Commissural diameter (cm)	3.53±0.51	3.63±0.42	0.1±0.61	0.499
Anterior leaflet area (cm^2)	5.82±1.13	6.29±1.37	0.47±1.69	0.273
Posterior leaflet area (cm^2)	5.65±1.58	4.88±1.65	0.76±1.19	<0.05
Anterior leaflet length (cm)	2.18±0.39	2.4±0.32	0.23±0.42	<0.05
Posterior leaflet length (cm)	1.53±0.51	1.27±0.33	0.25±0.43	<0.05
Posterior leaflet angle (°)	39.53±8.53	39.3±7.27	0.25±0.43	0.922
Aao-AP angle (°)	127.24±15.48	133.89±15.83	6.66±15.70	0.099
Dynamics				
Annular displacement (mm)	6.59±1.84	7.59±2.15	1±1.8	<0.05
Tenting volume fraction (%)	38.06±19.98	33.85±18.29	4.21±23.55	0.486
Annulus area fraction (%)	4±1.67	5.3±2.03	1.3±2.4	0.052

Data are presented as mean ± standard deviation. AP, anteroposterior, AL-PM, anterolateral-posteromedial.

ght at follow-up correlated with the 3D LA minimum and maximal volumes (r 0.642, p=0.007 and r 0.696, p=0.004, respectively), but did not correlate with the LA ejection fraction and LV 3D measured volumes and ejection fraction (Table 2). Similarly, the posterior leaflet length and area correlated with LA minimum and maximal volume (r 0.804, p=0.000 and r 0.835, p=0.000), but not with LA ejection fraction and LV 3D measured volumes and ejection fraction.

DISCUSSION

We analyzed the MV geometry using 3D echocardiography in patients early after acute STEMI and after 4 years of follow-up. To our knowledge this is the first study to describe the MV geometrical changes longitudinally during such a long period of time.

We describe novel insights regarding the alteration of MV geometry over time. First, the MV annulus dimensions (AP and AL-PM diameter, annulus circumference and area) remain unchanged, except for the annulus height which gets smaller in time, resulting in a flatter annulus late after MI. Second, the posterior leaflet length and area are getting smaller, while the anterior leaflet area remains constant. The tenting height and tenting area are getting smaller in time. Third, the MV geometrical changes over time correlate with LA volumes, but not with the LV volumes and ejection fraction. Fourth, the MV geometrical parameters are not significantly different in patients with compared to patients without IMR, both early and late after STEMI. Similarly, the MV geometrical parameters are not significantly different in patients with anterior compared to patients with non-anterior location of the infarction.

MITRAL ANNULUS GEOMETRY

Recent studies using 3D echocardiography have shown that in the setting of acute STEMI, patients with IMR have larger and flatter mitral annulus and larger systolic tenting compared to those without IMR[3,4]. In order to differentiate between the MV geometrical changes in acute vs chronic MR, distinct cohorts of patients were analyzed in the previous studies[3,4]. These studies have shown that chronic IMR is characterized by a flatter annulus, larger annular area and larger tenting volume[4]. However, none of these studies did repeatedly analyze the same cohort of patients. In our follow-up study, we confirm that the mitral annulus becomes progressively flatter over time, but the annular dimensions remain unchanged and the tenting height and area are getting smaller. Of note, none of the analyzed patients experienced aggravation of IMR severity over time. This may suggest that in the setting of acute STEMI, the tethering forces caused by LV dysfunction result in a higher tenting height, which is getting smaller over time in a process of "healing" of the MV, associated with LV dysfunction improvement.

MITRAL LEAFLETS

It was demonstrated that leaflets surface is significantly larger in chronic IMR compared to acute IMR[3,4]. Chaput et al. demonstrated that the mitral leaflet area increases in response to chronic tethering in patients with inferior wall-motion abnormality and dilated cardiomyopathy[7]. In some patients, an insufficient leaflet area relative to that demanded by tethering geometry results in significant MR (a leaflet-to-closure area ratio <1.7 was associated with significant MR).

Interestingly, we found that in the absence of severe IMR, the posterior leaflet length and area are actually

Table 2. The relation between follow-up mitral valve geometry parameters and left atrial three-dimensional volumes and ejection fraction

MV geometry parameter	LA minimum volume		LA maximal volume		LA ejection fraction	
	r	p	r	p	r	p
Tenting height	0.642	0.007	0.696	0.004	0.340	0.197
Tenting area	0.719	0.002	0.814	0.001	0.394	0.131
Posterior leaflet area	0.804	0.000	0.835	0.000	0.273	0.306
Posterior leaflet length	0.794	0.000	0.850	0.000	0.312	0.239

Data are presented as mean ± standard deviation. MV mitral valve, LA left atrium getting smaller over time. However, it is difficult to discern whether this finding reflects an absolute decrease of leaflet surface, or it is a pseudo-shortening due to decrease exposure for systolic contouring of posterior leaflet in the context of improved tenting parameters.

RELATIONSHIP BETWEEN MV GEOMETRY AND LV AND LA PARAMETERS

We have demonstrated that late after STEMI, higher values of tenting height and area correlate with 3D LA volumes, but not with 3D LV volumes or ejection fraction. This raises the question whether the MV geometrical conformation is more dependent on the LA morphology than on the LV volumes and function. The concept of atrial functional mitral regurgitation is currently regarded as distinct from the secondary mitral regurgitation which appears as a consequence of LV deformation[8]. Future studies are needed to establish the intimate relationships between MV geometrical distortion, LV and LA morphology and function.

LIMITATIONS AND STRENGTHS

The analyzed cohort was rather small, which may have resulted in an underestimation of some of the MV geometrical changes, from a statistical point of view. However, the longitudinal observation and repeated examination of the same cohort of patients permitted the unique opportunity to characterize the MV geometrical changes over time.

The severity of IMR may aggravate, may improve or may remain unchanged over time[9]. In our study, IMR did not aggravate, nor improved, and this may be explained by the low number of analyzed patients. Although a significant proportion of patients had mild or moderate IMR, none of them had severe MR. We may suspect that in the presence of severe MR, the MV geometrical changes may be significantly different.

CONCLUSION

Three-dimensional echocardiographic assessment of the MV permits detailed description of geometrical changes over time. MV geometry changes years after MI independently of the presence or severity of IMR. The MV healing process consists in annulus flattening associated with improved tenting. Further studies are needed to explore the intimate relationship between MV remodeling and LA morphology.

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Compliance with ethics requirements:

The authors declare no conflict of interest regarding this article.

The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

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