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ISCHEMIC MITRAL REGURGITATION: PROBLEM EXTENT IN CARDIOVASCULAR SURGERY CLINIC

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ABSTRACT

The aim of the study was to evaluate the prevalence, etiology, mechanisms and severety of all cases of MR, including IMR, in the patients population with suspected or proved CAD before coronary arteries evaluation and surgery or intervention.

Materials and methods: The study prospectively included 370 patients with verified or suspected (angina pectoris suspicion or manifested CHF) CAD of all clinical forms (stable, unstable, post-AMI, prior revascularization, etc.). MR evaluation by TTE included examining type of MR (organic or functional, Carpentier type) and its severity by vena contracta (VC) width and establishing effective regurgitant orifice (ERO) and regurgitant volume (RVol) by PISA method according to existing guidelines. Additional criteria (left atrium (LA) dimensions, LV diastolic filling and filling pressure markers, pulmonary veins flow and secondary pulmonary hypertension and right chambers involvement, etc.) were also widely used.

Results: Majority of all patients were men – 280 out of 370 pts (75.7%). Mean age of pts was 62.4±8.96 years, and men were in general significantly younger (61.5±9.2 vs. 65.3±7.6 years, p=0.0004). 145 (39.2%) pts had verified AMI previously (126 men and 19 women, p<0.0001). 22 (5.95%) pts previously underwent CABG surgery (19 men and 3 women, p<0.0001), and 99 patients – PCI with coronary stenting (81 men and 18 women, p<0.0001). 42 (11.3%) pts proved to have no significant CAD as per CAG results: 24 (57.1%) pts had no significant cardiac pathology at all, 12 (28.6%) pts had uncomplicated essential hypertension, 5 (11.9%) pts had non-coronary dilated cardiomyopathy (DCM) and 1 (2.4%) pt had non-obstructive hypertrophic cardiomyopathy (HCP) with clean coronary arteries. In patients with CAD MR is a frequent finding (up to one-half of the studied population) regardless of gender. Predominant majority (84.1%) of MR according to TTE findings is mild (grade I), without significant influence upon heart load and remodeling, and, thus, requiring no additional surgeon interventions. Most of cases of such pathological MR resolved after myocardial revascularization or sustained without dynamics being physiological (13.2% of all MR cases). Most of moderate-to-severe MR cases were classified as IMR, being accompanied by appropriate LV remodeling features, requiring revascularization and/or mitral valvuloplasty or replacement (all cases of severe IMR or organic MR). Correlations results of MR ERO and RVol with certain heart chambers remodeling and load indices seem to make them a "gold standard" for MR severity evaluation, especially in CAD patients with potential indications for MV surgery that should accompany surgeon revascularization, as it is widely accepted today.

Conclusions: In the patients with various forms of chronic and acute CAD IMR is a frequent finding, but the majority of MR cases are mild and requiring no additional interventions. No gender difference in MR prevalence were found. Severe MR cases in all CAD patients population are rather rare (below 10%), but always require surgical repair. Moderate-to-severe IMR is the most frequent (approximately 75%) etiology for significant MR in CAD patients, requiring close TTE follow-up for optimal intervention timing on the basis of left and right chambers remodeling and load indices. MR ERO and RVol are trustworthy quantitative MR severity indices, significantly correlating with main LV and LA remodeling and load indices, as well as with some secondary right chambers overload predictors.

KEY WORDS: coronary arteries disease, ischemic mitral regurgitation, transthoracic echocardiography

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INTRODUCTION

Chronic ischemic mitral regurgitation (IMR) is a subtype of secondary mitral regurgitation (MR) and a complication of coronary arteries disease (CAD). It is a pathophysiological phenomenon of insufficient mitral cusps coaptation mostly due to global or local left ventricle (LV) geometry impairment with mitral valve (MV) apparatus deformation. Most of IMR cases are secondary to LV geometry alterations [1, 2] in the patients with ischemic cardiomyopathy (ICM), chronic or acute (postinfarction), while primary organic cases due to mitral chords rupture during acute myocardial infarction are relatively rare [3]. Mechanisms of IMR were widely described [1,2,4,5], being usually referred to as type IIIb Carpentier [1]. Although IMR is associated with significant (>70%) of at least one trunk coronary artety [4], the term IMR itself not necessarily include real current myocardial ischemia, but often characterizes certain clinical situation of postischemic changes, leading to global or regional pathological remodeling progression [5]. Detailed studies with thorough echocardiography (EchoCG) evaluation spotted various LV remodeling prognostic markers of reverse remodeling and IMR and congestive heart failure (CHF) progression [1,2,6].

Overall prevalence of all causes MR in Europe remains high, being the second most common valve disease that affect up to one third of population [4]. IMR is described as the second most common cause of MR (25%) after degenerative (60%) and far ahead of rheumatic MR (12%),

Table 1. General characteristics of study group

• Total – 370 pts
Men – 280 (75.7%)
Women – 90 (24.3%), p<0.0001
• Age – 62.4±8.96 yrs.
Men – 61.5±9.2
Women – 65.3±7.6, p=0.0004
• Prior AMI – 145 (39.2%)
Men – 126 (86.9%)
Women – 19 (13.1%), p<0.0001
• Prior CABG – 22 (5.95%)
Men – 19 (86.4%)
Women – 3 (13.6%), p<0.0001
• Prior PCI / coronary stenting – 99 (26.8%)
Men – 81 (81.8%)
Women – 18 (18.2%), p<0.0001
• CAD not verified by CAG results – 42 (11.3%)
Healthy heart – 24 (57.1%)
Uncomplicated essential hypertension – 12 (28.6%)
Non-coronary DCM – 5 (11.9%)
Non-obstructive HCM – 1 (2.4%)

progressively increasing recently. Up to 40% of patients after AMI are also diagnosed with IMR by EchoCG [7].

Surgery remains the basis for IMR treatment in most cardiac surgery units due to unsatisfactory medication treatment results and significant prognosis worsening in case of marked IMR. Namely, IMR is associated with three-times increase of clinically significant CHF and 1.6 times mortality increase in the next 5 years [8]. Mortality rates over 5 – 7 years follow-up in cases of conservative treatment remains high, constituting 60 – 100% depending on IMR severity, CAD severity and LV remodeling advance [6]. There is a strong evidence that CABG or PCI themselves with or without MV annuloplasty lead to significant reverse left chambers remodeling and significantly improve prognosis in CAD patients [9], unless MR is severe and/or organic, definitely requiring surgeon repair. Still, today we lack detailed prospective evidence and focus of international guidelines on IMR.

THE AIM

The aim of the study was to evaluate the prevalence, etiology, mechanisms and severety of all cases of MR, including IMR, in the patients with suspected or proved CAD, who were to undergo possible revascularization.

MATERIALS AND METHODS

The study was approved by local ethics committee. The materials, used in the study, do not violate the principles of bioethics and can be published. All patients participating in the study gave their consent and signed an approved informed consent form (ICF).

The study prospectively included 370 patients with verified or suspected (angina pectoris suspicion or manifested CHF) CAD of all clinical forms (stable, unstable, post-AMI, prior revascularization, etc.). No exclusion criteria for MR evaluation were set. During and after diagnostic work-up and coronary angiography (CAG) and/or revascurarization standard none of the patients was diagnosed with perioperative myocardial infarction. Medication treatment in all the post-infarction patients included aspirin and/or clopidogrel, statins, beta-blockers, ACE inhibitors or sartans, and nitrates, if indicated. All patients underwent transthoracic EchoCG (TTE) prior any interventions and after, if indicated. Program of the study included X-ray contrast CVG and Doppler TTE with LV myocardial speckle-tracking (STE).

CAG was conducted and interpreted by trained physicians A 50% or more reduction of the luminal diameter in 2 orthogonal projections of a major coronary artery or one of its major branches or a bypass graft was considered to be significant for CAD.

During TTE with STE recordings and calculations of different parameters, including LV chamber volumes and EF, were performed according to existing Guidelines [10]. MR evaluation included examining type of MR (organic or functional, Carpentier type) and its severity by vena contracta (VC) width and establishing effective regurgitant orifice (ERO) and regurgitant volume (RVol) by PISA method according to existing guidelines [1,2]. Additional criteria (left atrium (LA) dimensions, LV diastolic filling and filling pressure markers, pulmonary veins flow and secondary pulmonary hypertension and right chambers involvement, etc.) were also widely used [1,2,4].

Comparison of different parameters was performed using multiple regression analysis with 95% confidence interval and correlation analysis.

RESULTS AND DISCUSSION

Majority of all patients were men – 280 out of 370 pts (75.7%). Mean age of pts was 62.4±8.96 years, and men were in general significantly younger (61.5±9.2 vs. 65.3±7.6 years, p=0.0004). 145 (39.2%) pts had verified AMI previously (126 men and 19 women, p<0.0001). 22 (5.95%) pts underwent CABG surgery (19 men and 3 women, p<0.0001), and 99 patients previously underwent PCI with coronary stenting (81 men and 18 women, p<0.0001). 42 (11.3%) pts proved to have no significant CAD as per CAG results: 24 (57.1%) pts had no significant cardiac pathology at all, 12 (28.6%) pts had uncomplicated essential hypertension, 5 (11.9%) pts had non-coronary dilated cardiomyopathy (DCM) and 1 (2.4%) pt had non-obstructive hypertrophic cardiomyopathy (HCP) with clean coronary arteries (Table 1).

182 (49.2%) pts had MR according to TTE results with no significant difference between genders (142 (50.7%) men vs. 40 (44.4%) women, p=0.30).

According to etiology MR was classified as:

- trivial (physiological) MR – minimal regurgitant flow on intact MV in the patients with normal left chambers and no regional contractility abnormalities or ischemic remodeling signs;
- ischemic MR (IMR) – any severity MR in the patients with verified CAD and obvious ischemic LV and/or LA remodeling (dilation, regional wall contraction abnormalities, obvious papillary muscles dysfunction, MV tethering and restriction, etc.);
- sunctional secondary MR – left chambers and mitral ring dilation with MV tenting in the absence of verified CAD due to DCM, atrial fibrillation, etc.);
- organic (primary) MR of any etiology (Barlow disease, rheumatic, flail MV, etc.).

Organic MR was rare in the studied group – 9 (4.95%) cases with no gender differences (4 men vs. 5 women, p=0.64). Of them only 4 pts. had verified CAD, of which 2 had stable insignificant CAD (50% LAD in one case and patent stents in the other), while 2 other required CABG surgery due to multi-vessel disease, but had obviously organic etiology of MR (flail P2 segment due to Barlow disease and mild rheumatic MR combined with mild stenosis) (Table 2). Only 3 patients required urgent MV surgery due to severe decompensated MR with clinically significant CHF due to flail MV. Therefore, all these cases of obviously non-ischemic primary MR were no further analyzed.

Table 2. Etiology and severity of primary organic MR in the studied group.

Severity (Total 9 (4.95%) cases)
• Grade I (mild) – 4 (44.5%)
• Grade II (moderate) – 2 (22.2%)
• Grade III (severe) – 3 (33.3%)
Etiology
• Rheumatic – 3 (33.3%)
Combined mitral without prevalence grade 1 (mild)
Combined mitral with MR prevalence grade 2 (moderate)
• Barlow disease (MV prolapse) – 6 (66.7%)
With MR grade 1 (mild) – 1 (11.1%)
With MR grade 2 (moderate) – 2 (22.2%)
Flail MV (chords rupture) – 3 (33.3%)

Table 3. Correlation of MR severity indices with left and right chambers function, remodeling and overload markers.

Index	MV ERO	MV RVol	Significance between two correlation coefficients
LV iEDD, cm/m^2	**r=0.222, p=0.0024**	r=0.347, p<0.0001*	p=0.20
LV iEDV, ml/m^2	**r=0.193, p=0.0085**	**r=0.353, p<0.0001**	p=0.10
LV iESV, ml/m^2	r=0.111, p=0.13	r=0.234, p=0.0014	p=0.23
LAs, cm	r=0.242, p=0.0009	r=0.481, p<0.0001	p=0.0091
LAV, ml	r=0.354, p<0.0001	r= 0.639, p<0.0001	p=0.0003
iLAV, ml/m^2	r= 0.390, p<0.0001	r= 0.679, p<0.0001	p=0.0001
LV EF, %	r= – 0.02, p=0.77	r= – 0.10, p=0.16	p=0.45
E/A	**r=0.219, p=0.0028**	**r=0.404, p<0.0001**	p=0.052
E/E'	r=0.093, p=0.21	r=0.077, p=0.30	p=0.88
LV diastolic dysfunction grade	**r=0.192, p=0.009**	**r= 0.344, p<0.0001**	p=0.12
PA SBP, mm Hg	r=0.104, p p=0.16	**r= 0.244, p=0.0009**	p=0.17
PA Mean BP, mm Hg	r=0.087, p=0.25	**r=0.225, p=0.0021**	p=0.18
RA short, cm	r=0.073, p=0.33	**r=0.176, p=0.017**	p=0.32
RA long, cm	r=0.005, p=0.94	r=0.011, p=0.88	p=0.96
iRAV, ml/m^2	r=0.112, p=0.13	**r=0.198, p=0.0007**	p=0.41
RV basal EDD, cm	r=0.126, p=0.088	**r=0.227, p=0.002**	p=0.32
RV wall, cm	r=0.117, p=0.11	**r=0.24, p=0.001**	p=0.23
RV TAPSE, cm	r=0.117, p=0.11	r= – 0.03, p=0.72	p=0.16
RV S', cm/s	r= – 0.01, p=0.92	r= 0.023, p=0.75	p=0.76
IVC, cm	r= 0.125, p=0.09	**r= 0.176, p=0.017**	p=0.62
CVP, mm Hg	r= 0.07, p=0.34	r= 0.119, p=0.11	p=0.64
LV GLS, %	r= – 0.03, p=0.66	r= – 0.01, p=0.92	p=0.85
RV GLS, %	r= – 0.02, p=0.79	r= – 0.01, p=0.91	p=0.93
TR ERO, cm^2	**r=0.191, p=0.01**	**r=0.288, p<0.0001**	p=0.33
TR RVol, ml	**r=0.216, p=0.0033**	**r=0.323, p<0.0001**	p=0.28

* – bold – weak to moderate significant correlation and significant difference between correlation coefficients.

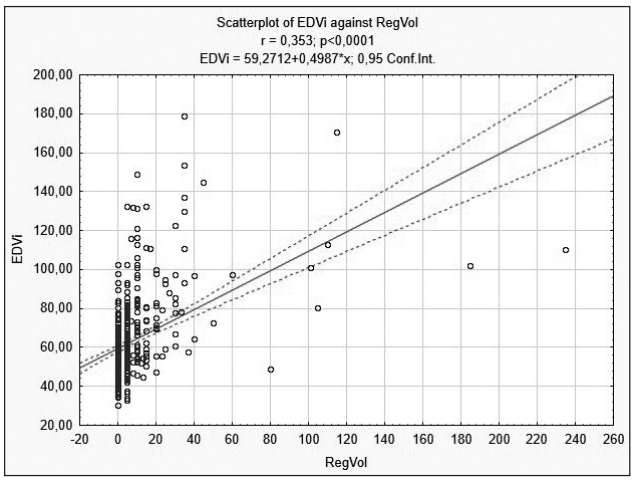

Fig. 1. Weak-to-moderate correlation between MR RVol and LV iEDV (r=0.353; p<0.0001).

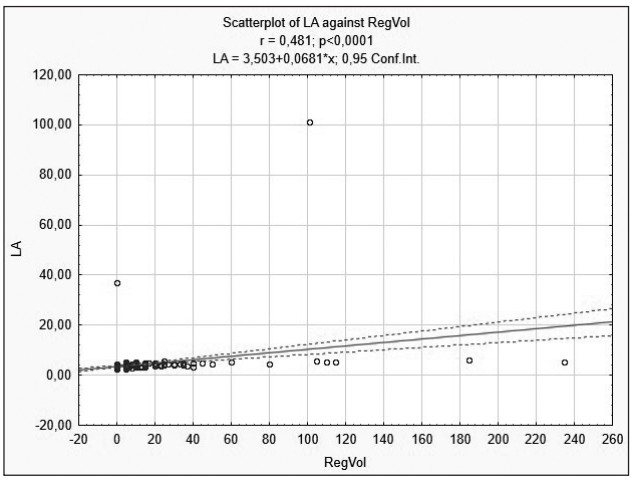

Fig. 2. Weak-to-moderate correlation between MR RVol and LA end-systolic diameter (r=0.481; p<0.0001).

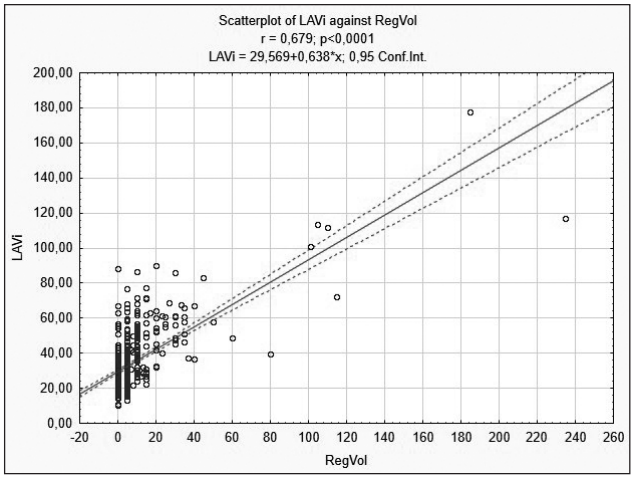

Fig. 3. Moderate correlation between MR RVol and iLAV (r=0.679; p<0.0001).

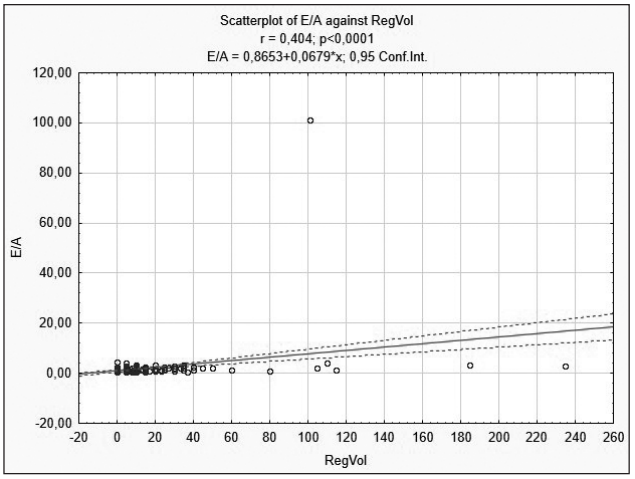

Fig. 4. Weak-to-moderate correlation between MR RVol and LV diastolic filling (E/A ratio) (r=0.404; p<0.0001).

Overwhelming majority of all registered MR cases were patients with mild (grade I) MR – 153 (84.1%) cases with no significant difference between genders (122 (85.9%) men vs. 31 (77.5%) women, p=0.060). Although women showed significantly higher quantitative extent of MR with higher ERO (0.17±0.54 vs. 0.08±0.04 cm^2, p=0.0058) and RVol (9.9±6.2 vs. 8.3±4.5 ml, p=0.0082), there was no gender differences in the etiology of mild MR. There were 24 (15.7%) cases of trivial physiological MR, 11 (7.2%) cases of secondary non-ischemic MR and 4 (2.6%) cases of mild primary organic MR (rheumatic or due to MV prolapse). The majority (114 (74.5%) cases) of mild MR (grade I) were qualified as ischemic MR in the patients with verified CAD and obvious ischemic LV and/or LA remodeling. Still, it did not require additional surgeon intervention, as well as moderate MR grade 2.

Significant (grades 2 and 3) MR was not so frequent.

There were only 16 (8.8%) cases of moderate (grade 2) MR, more frequent in women (20.0% vs. 5.6%, p=0.044) with no significant difference in ERO (0.2±0.00 cm^2) and RVol (31.4±4.2 ml). Majority of moderate MR was IMR – 12 (75.0%) cases.

There were only 13 (7.1%) cases of severe MR (grade 3) with ERO 0.59±0.40 cm^2 and RVol 86.9±62.8 ml. All cases were accompanied by marked symptomatic CHF, corresponding LV and LA overload and marked secondary pulmonary hypertension, and required surgery. Most of cases (9 (75.5% pts) were qualified as IMR with indications for CABG combined with valvuloplasty or MV replacement (MVR).

Both MR ERO and RVol showed to weakly to moderately but significantly correlate main LV and LA remodeling indices, especially RVol, which significantly correlated with indexed to body surface area (BSA) LV end-diastolic diameter (EDD) and volume (EDV), and especially with LA end-systolic diameter (LAs) and absolute and BSA-indexed LA volume (LAV and iLAV). Also, significant correlation between LV diastolic dysfunction grade and E/A ratio on one hand, and MR RVol, on the other. Correlation between MR RVol and right-sided overload indices (pulmonary artery (PA) systolic (SBP) and mean pressure and right ventricle (RV) and atrium (RA) diameters) were weak but significant, which shows that MR indices might also show prognostic about indices of pulmonary hyperten-

sion and right chambers load and function, including significant weak-to-moderate correlation with indiced of secondary tricuspid regurgitation (TR) (Table 3). In general, MR RVol correlated with LV and LA remodeling and load indices better than MR ERO (Fig. 1 – 4). No correlation was found between indices of MR severity and LV and RV systolic function indices, namely LV EF and LV and RV global longitudinal strain (GLS) by STE.

Also, we found no significant correlation between VC width and most of the studied heart chambers remodeling and load indices.

According to the results of our study, involving 370 patients with CAD MR is a frequent finding (up to one-half of the studied population) regardless of gender. Predominant majority (84.1%) of MR according to TTE findings is mild (grade I), without significant influence upon heart load and remodeling, and, thus, requiring no additional surgeon interventions. Most of cases of such pathological MR resolved after myocardial revascularization or sustained without dynamics being physiological (13.2% of all MR cases).

Most of moderate-to-severe MR cases were classified as IMR, being accompanied by appropriate LV remodeling features, such as postinfarction aneurysms, scars, marked regional contraction abnormalities, LA and mitral annulus dilation, LV global and regional dilation with MV tethering, requiring revascularization and/or mitral valvuloplasty or replacement (all cases of severe IMR or organic MR).

Correlations results of MR ERO and RVol with listed above heart chambers remodeling and load indices seem to make them a "gold standard" for MR severity evaluation, especially in CAD patients with potential indications for MV surgery, that should accompany surgeon revascularization, as it is widely accepted today. At the same time, VC as per our experience, is much less validated, and can remain only as empirical qualitative method, that should not be used for quantifying MR severity without other indices.

Prospective inclusion of patients in the absence of inter-observer variability (all TTE were performed by the same sonographer on one EchoCG machine) allowed to avoid typical inter-observer study limitations.

CONCLUSIONS

In the patients with various forms of chronic and acute CAD IMR is a frequent finding, but the majority of MR cases are mild and requiring no additional interventions. No gender difference in MR prevalence were found. Severe MR cases in all CAD patients population are rather rare (below 10%), but always require surgical repair. Moderate-to-severe IMR is the most frequent (approximately 75%) etiology for significant MR in CAD patients, requiring close TTE follow-up for optimal intervention timing on the basis of left and right chambers remodeling and load indices. MR ERO and RVol are trustworthy quantitative MR severity indices, significantly correlating with main LV and LA remodeling and load indices, as well as with some secondary right chambers overload predictors.

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Conflict of interest:

The Authors declare no conflict of interest.

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