Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.elsevier.com/locate/medici

Original Research Article

Functional (ischemic) mitral regurgitation in acute phase of myocardial infarction: Associated clinical factors and in-hospital outcomes

Živilė Valuckienė *, *Dominyka Urbonaitė*, *Renaldas Jurkevičius*

Department of Cardiology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

ARTICLE INFO

Article history:
Received 8 March 2014
Accepted 9 February 2015
Available online 25 March 2015

Keywords:
Mitral regurgitation
Myocardial infarction
In-hospital outcome

ABSTRACT

Background and objective: Mitral regurgitation (MR) after myocardial infarction (MI) carries adverse prognosis. The objective of this study was to assess the impact of functional MR on adverse in-hospital outcomes in acute MI.

Materials and methods: A total of 569 patients with first ever acute MI were divided into three groups: no MR, mild MR (regurgitant orifice area <0.2 cm^2) and moderate-severe MR group (regurgitant orifice area more or equal >0.2 cm^2). Clinical profile and in-hospital outcomes were compared among the groups.

Results: Patients with increasing grade of MR were elder ($P < 0.001$), more likely to be female ($P = 0.003$), have atrial fibrillation ($P < 0.001$), higher peak C-reactive protein values ($P = 0.001$), multivessel coronary artery disease ($P < 0.001$), and less likely to have dyslipidemia ($P = 0.029$). Ejection fraction, age, atrial fibrillation and left ventricular end diastolic diameter index were independent predictors of moderate and severe MR ($P < 0.001$). In hospital cardiac death and decompensated heart failure was more prevalent in moderate-severe MR group.

Conclusions: Moderate and severe MR in acute MI is related to age, atrial fibrillation, increased left ventricular diastolic dimensions and decreased ejection fraction. Moderate and severe, but not mild MR is an important clinical contributor to in-hospital cardiac death.

* *Corresponding author at*: Department of Cardiology, Medical Academy, Lithuanian University of Health Sciences, Eivenių 2, 50161 Kaunas, Lithuania.
E-mail address: z.valuckiene@gmail.com (Ž. Valuckienė).

Peer review under the responsibility of the Lithuanian University of Health Sciences.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.medici.2015.02.003

1. Introduction

Ischemic mitral regurgitation (MR) after myocardial infarction (MI) is a recognized adverse prognostic factor known to account for increased risk of adverse patient outcomes: it is an independent predictor of increased mortality, risk of heart failure and death at long-term follow-up [1,2]. Although MR after MI is a frequently reported echocardiographic finding, significant (moderate and severe) MR is less prevalent [3]. Recently even mild MR was recognized as an important risk factor contributing to increased risk of heart failure and death after MI during a long-term follow up [2,4].

A great proportion of lethal post MI complications occur in acute phase of myocardial infarction or during the hospitalization period, and the role of ischemic MR in this setting is being explored [1,5,6].

Reported incidence of significant (moderate and severe) MR after MI ranges between 6% and 12% [3,7,8]. Recognition of ischemic MR and pitfalls of its estimation by angiographic studies and semi-quantitative color flow Doppler echocardiographic imaging rises a need to reassess the prevalence of ischemic MR by established quantitative doplerographic measures according to recent international guidelines for valve function assessment [9].

The aims of this study are to assess the incidence of mitral regurgitation in patients with myocardial infarction, to determine associated clinical factors, and the impact of MR on in-hospital cardiac death.

2. Materials and methods

Retrospective analysis of electronic health records database was performed to identify patients, who presented and were treated for suspected acute myocardial infarction at Hospital of Lithuanian University of Health Sciences (HLUHS) Kaunas clinics in the year 2012: 869 such cases were identified. Only patients with confirmed diagnosis of MI who met the diagnostic criteria of European Society of Cardiology third definition of myocardial infarction [10] and had undergone in-hospital departmental echocardiographic examinations were further considered for inclusion in the study (812 cases). The echocardiographic reports were reviewed for adequate data and quality assessment. The following exclusion criteria were applied: reported suboptimal image quality for valve function assessment, structural hemodynamically significant aortic valve disease, structural mitral valve abnormalities, left sided heart valve replacement/repair, mechanical complications of myocardial infarction, known dilated, hypertrophic or storage cardiomyopathies, and previously known mitral regurgitation. Application of aforementioned exclusion criteria resulted in final study population comprising 731 patients with confirmed MI (with or without ST segment elevation on ECG) and adequate departmental echocardiographic assessment of cardiac structures and valve function.

The following clinical data were obtained from medical records: vital parameters (arterial blood pressure and heart rate upon admission), medical history (arterial hypertension, history of prior MI, dyslipidemia, diabetes mellitus, ischemic stroke, and atrial fibrillation), biochemical markers (peak troponin I, peak C-reactive protein (CRP) values, serum creatinine, lipid profile). Dyslipidemia was defined as elevated total (>5.2 mmol/L) or low-density lipoprotein (LDL) level (>2.59 mmol/L), or low levels of high-density lipoprotein (HDL) cholesterol (<1.55 mmol/L). Echocardiographic findings (index of left ventricular end diastolic diameter (LV EDDi), LV ejection fraction (EF), myocardial mass index (MMI), grade of mitral regurgitation), ECG criteria (ST segment elevation, Q wave formation, localization of MI, conduction and rhythm disturbances), coronary angiography findings, percutaneous coronary intervention results, and clinical course (heart failure class according to Killip, in-hospital treatment duration and outcomes) have also been recorded.

At HLUHS Kaunas Clinics mitral regurgitation is routinely quantified according to the recommendations provided by European Society of Echocardiography, and reported as none (grade 0), mild (grade I, regurgitant orifice area (ROA) $< 0.2\ cm^2$), moderate (grade II, ROA 0.2–0.3 cm^2), or severe (grade III–IV, ROA $\geq 0.3\ cm^2$ or $\geq 0.4\ cm^2$ respectively) [7]. Based on reported mitral regurgitation degree all patients were divided into three groups: no mitral regurgitation group (no identifiable or measurable MR), mild mitral regurgitation (M-MR) group (grade I) and moderate-severe mitral regurgitation (M/S-MR) group (grade II–IV).

Statistical analysis was performed with SPSS 21.0 statistics package. The data were expressed as mean ± standard deviation or median for continuous variables, and number (%) for categorical variables. Clinical and other characteristics were compared among the groups of mitral regurgitation with chi-square test for categorical variables and ANOVA test for linear variables. Intragroup comparisons for categorical variables were performed with Z test, while quantitative variables within the groups were compared by Tukey and Dunnett's T_3 tests if dispersions were equal or not, respectively. In addition, logarithm function and Tukey test were used to compare means of triglycerides within the groups of mitral regurgitation, where the distribution of triglycerides was not following the normal distribution. Multivariate logistic regression analysis was performed to assess the impact of selected risk factors to development of significant MR after adjusting for possible confounding factors. Univariate regression analysis was performed to explore predictors of in-hospital cardiac death.

3. Results

The final study population comprised 731 patients: 511 (69.9%) men and 220 (30.1%) women. The mean age of the patients was 65.37 ± 11.99 years (range 23–94 years). A total of 569 (77.8%) patients were treated for the first ever MI; 162 (22.2%), for repeated MI. In-hospital cardiac death occurred in 24 (3.3%) patients: 16 (2.8%) deaths were reported in the incidental first MI group, and 8 (4.9%) deaths in repeated MI group.

3.1. *Incidence and prevalence of MR*

In the general MI population (n = 731), varying degrees of MR were reported in 629 (86%) patients, and no detectable or measurable MR was found in 102 (14%) patients. Prevalence

Table 1 – Prevalence of mitral regurgitation after myocardial infarction.

	Prior MI population, $n = 162$	First MI population, $n = 569$	P
No-MR	17 (10.5)	85 (14.9)	NS
M-MR	97 (59.9)	386 (67.8)	NS
M/S-MR	48 (29.6)	98 (17.2)	0.005

Values are number (percentage). Prior MI population, cases of known prior myocardial infarction (MI); first MI population, cases of incidental first ever MI; no-MR, no mitral regurgitation (MR) group; M-MR, mild MR group; M/S-MR, moderate and severe MR group; NS, not significant.

and incidence of MR in prior MI population and incidental MI populations is presented in Table 1. Moderate and severe MR was found to be significantly more prevalent in prior MI population compared to the first incidental MI population (29.6% vs. 17.2% respectively, $P = 0.005$).

3.2. *Demographic and clinical profile*

Basic demographic and clinical characteristics were compared among the three groups of mitral regurgitation in the first ever MI population ($n = 569$). The findings are presented in Table 2.

Patients with increasing grade of MR were progressively elder ($P < 0.001$). Patients in M/S-MR group were more likely to be female ($P = 0.003$), had lower systolic ($P = 0.009$) and diastolic blood pressure upon presentation ($P = 0.014$), higher peak CRP values ($P = 0.001$), and lower plasma triglyceride levels ($P = 0.004$) as compared to no MR and M-MR groups. There was no statistically significant difference in these parameters between no-MR and M-MR groups. Dyslipidemia was less likely to be present in M/S-MR group compared to the no-MR group ($P = 0.029$) while the M-MR group was found to be statistically no different in the prevalence of dyslipidemia from either other MR group. Total cholesterol ($P = 0.002$) and LDL levels ($P = 0.007$) were significantly higher in no MR compared to both MR groups (M-MR and M/S-MR). Although proportionately more cases of M/S-MR group fell to the highest troponin rise category than in any other MR subgroup, statistically significant difference is attributable to maximal troponin rise in the moderate range (tertile 2): more cases of no MR group had maximal troponin rise within the moderate range (55.3%) as compared to M/S-MR group (18.4%). There was no statistically significant association found between the presence of MR and arterial hypertension, diabetes, renal failure or history of ischemic stroke; however there was a strong association between moderate and severe mitral regurgitation and history or presence of atrial fibrillation (including both its paroxysmal and chronic forms, $P < 0.001$).

Table 2 – Demographic and clinical profile of 569 patients with first ever acute myocardial infarction grouped by mitral regurgitation degree.

Variable	No-MR ($n = 85$)	M-MR ($n = 386$)	M/S-MR ($n = 98$)	P
Demographics				
Age, years	59.8 ± 11.2^{a}	64 ± 11.7^{b}	71.5 ± 10.9^{c}	<0.001
Female:male ratio	$1:4.31^{a}$	$1:2.33^{a,b}$	$1:1.39^{b}$	0.003
Risk factor profile, comorbidities				
Obesity ≥30 kg/m^2, *n* (%)	18 (21.2)	94 (24.4)	15 (15.3)	0.152
Hypertension, *n* (%)	76 (89.4)	329 (85.2)	87 (88.8)	0.454
Dyslipidemia, *n* (%)	$79 (92.9)^{a}$	$347 (89.9)^{a,b}$	$80 (81.6)^{b}$	0.029
Diabetes, *n* (%)	10 (11.8)	58 (15)	15 (15.3)	0.725
Renal insufficiency, *n* (%)	4 (4.7)	14 (3.6)	8 (8.2)	0.158
Atrial fibrillation, *n* (%)	$7 (8.2)^{a}$	$37 (9.6)^{a}$	$23 (23.5)^{b}$	<0.001
History of ischemic stroke, *n* (%)	6 (7.1)	12 (3.1)	8 (8.2)	0.05
Vital parameters				
Heart rate upon admission, bpm	77.0 ± 17.7	74.9 ± 14.9	77.7 ± 17.9	0.231
Systolic blood pressure, mm Hg	144.0 ± 22.8^{a}	140.4 ± 23.5^{a}	134.3 ± 24.1^{b}	0.009
Diastolic blood pressure, mm Hg	85.8 ± 11.6^{a}	84.3 ± 13.4^{a}	80.5 ± 13.3^{b}	0.014
Biochemical profile				
Peak troponin, *n* (%)				
Tertile 1	$19 (22.35)^{a,b}$	$134 (34.7)^{a,b}$	$37 (37.7)^{a,b}$	
Tertile 2	$47 (55.3)^{a}$	$122 (31.6)^{a,b}$	$18 (18.4)^{b}$	0.019
Tertile 3	$19 (22.35)^{a,b}$	$130 (33.7)^{a,b}$	$43 (43.9)^{a,b}$	
Peak CRP, n^{d} (%)	$19 (22.4)^{a}$	$120 (31.1)^{a}$	$49 (50)^{b}$	0.001
Total cholesterol, mmol/L	5.74 ± 1.4^{a}	5.3 ± 1.2^{b}	5.0 ± 1.1^{b}	0.002
Triglycerides, mmol/L	1.8 ± 1.2^{a}	1.6 ± 1.3^{a}	1.3 ± 0.8^{b}	0.004
HDL, mmol/L	1.1 ± 0.4	1.2 ± 0.4	1.3 ± 0.5	0.7
LDL, mmol/L	3.8 ± 1.2^{a}	3.4 ± 1.1^{b}	3.3 ± 1^{b}	0.007
Random plasma glucose on admission, mmol/L	7.1 ± 2.5	7.3 ± 2.8	7.5 ± 2.9	0.73

No-MR, no mitral regurgitation (MR) group; M-MR, mild MR group; M/S-MR, moderate and severe MR group; CRP, C-reactive protein; HDL, high-density lipoproteins; LDL, low-density lipoproteins.

[a,b,c] Difference is statistically significant between different letters, and insignificant between the same letters.

[d] *n* in tertile 3 (%).

Table 3 – Distribution of mitral regurgitation grade and localization of myocardial infarction.

Localization	No-MR	M-MR	M/S-MR
Anterior, *n* (%) (*n* = 280)	40 (14.3)	206 (73.6)	34 (12.1)
Inferior, *n* (%) (*n* = 264)	45 (17)	164 (62.1)	55 (20.8)
Posterior, *n* (%) (*n* = 17)	3 (17.6)	11 (64.7)	3 (17.6)
Lateral, *n* (%) (*n* = 10)	2 (20)	7 (70)	1 (10)

No-MR, no mitral regurgitation (MR) group; M-MR, mild MR group; M/S-MR, moderate and severe MR group; % within MI groups.

3.3. *Localization and type of MI*

In 11 of the 569 patients, the localization of MI was undefined due to lack of ischemic ECG changes or underlying Hiss bundle branch block, and coronary angiography was inconclusive for the culprit lesion (presence of angiographically significant coronary artery disease in more than one coronary artery territory). The presence and degree of MR was compared among the three groups of MR in 558 remaining patients with identifiable MI localization based on ECG and/or coronary angiography findings (Table 3).

There was no association found between MR grade and presence of pathological Q wave formation or ST segment elevation on ECG (Table 4). There were relatively few cases of isolated posterior (*n* = 17) and lateral (*n* = 10) MI; therefore, the incidence of MR was compared between anterior and inferior MI groups. M/S-MR was significantly more prevalent in inferior compared to anterior MI group (20.8% vs. 12.1%, *P* = 0.006), while more cases of mild MR were observed in anterior MI group. There was no impact of cardiac conduction disturbances or permanent cardiac pacing found on the presence of any degree of MR.

3.4. *Angiographic data*

All study patients had undergone coronary angiography (Table 5). Number of coronary vessels with angiographically significant lesions (coronary artery luminal stenosis by visual assessment equal to or greater than 70%) was higher in M/S-MR group compared to the no-MR and M-MR groups ($P < 0.001$). Patients in M/S-MR group were more likely to have triple vessel CAD compared to the no-MR and M-MR groups (*P* = 0.002). Left main coronary artery (LMCA) and right coronary artery (RCA) lesions were found to be strongly associated with the presence of moderate and severe MR ($P < 0.001$). There was no significant difference in MR grade distribution between successful and unsuccessful/not performed PCI subgroups.

Table 4 – MI localization and MR grade distribution.

	No-MR	M-MR	M/S-MR	P
Type of MI (*n* = 569)				
Q wave MI	50 (58.8)	218 (56.5)	63 (64.3)	0.372
STEMI	54 (63.5)	227 (58.8)	51 (52)	0.276
Localization of MI (*n* = 558)				
Anterior, n = 280	40 (14.3)	206 (73.6)*	34 (12.1)**	0.006
Inferior, n = 264	45 (17)	164 (62.1)*	55 (20.8)**	
Conduction disturbances (*n* = 569)				
Pacemaker	0 (0)	13 (3.4)	4 (4.1)	0.2
LBBB	2 (2.4)	31 (8)	10 (10.2)	0.11
RBBB	5 (5.9)	25 (6.5)	6 (6.1)	0.975

Values are number (percentage). No-MR, no mitral regurgitation (MR) group; M-MR, mild MR group; M/S-MR group, moderate and severe MR group; MI, myocardial infarction; STEMI, ST-segment elevation myocardial infarction; LBBB, left bundle branch block; RBBB, right bundle branch block.
* Difference is statistically significant between these two groups.
** Difference is statistically significant between these two groups.

3.5. *Echocardiographic determinants*

A graded association was found between MR grade, LV EDD index, MMI, and EF. Increasing LV EDD dimensions and MMI, and decreasing EF are strongly associated with greater MR ($P < 0.001$) (Table 6). There was no significant relation of the presence of mitral annular calcification and MR grade.

Table 5 – Angiographic data.

Data	No MR (*n* = 85)	M-MR (*n* = 386)	M/S-MR (*n* = 98)	P
Number of CA with significant lesions	1.7 ± 0.8[a]	1.8 ± 0.8[a]	2.1 ± 0.8[b]	<0.001
CAD, *n* (%)				
Single vessel CAD	39 (45.9)[a]	176 (45.6)[a]	26 (26.5)[b]	
Two vessel CAD	30 (35.3)	119 (30.8)	33 (33.7)	0.002
Triple vessel CAD	16 (18.8)[a]	91 (23.6)[a]	39 (39.8)[b]	
Location of significant coronary lesions, *n* (%)				
LMCA	1 (1.2)[a]	8 (2.1)[a]	10 (10.2)[b]	<0.001
LAD	60 (70.6)	291 (75.4)	72 (73.5)	0.641
LCx	36 (42.4)	187 (48.4)	55 (56.1)	0.171
RCA	51 (60)[a]	203 (52.6)[a]	74 (75.5)[b]	<0.001
PCI (% within MR groups), *n* (%)				
PCI successful, *n* = 462	68 (80)	317 (82.1)	77 (78.6)	0.691
PCI unsuccessful/not performed, *n* = 107	17 (20)	69 (17.9)	21 (21.4)	

No-MR, no mitral regurgitation (MR) group; M-MR, mild MR group; M/S-MR group, moderate and severe MR group; CA, coronary artery; CAD, coronary artery disease; LMCA, left main coronary artery; LAD, left anterior descending artery; LCx, left circumflex artery; RCA, right coronary artery; PCI, percutaneous coronary intervention. Difference is statistically significant between different letters (a, b), and insignificant between same letters.

Table 6 – Echocardiographic parameters.

Parameter	No-MR ($n = 85$)	M-MR ($n = 386$)	M/S-MR ($n = 98$)	P
LVEDD, mm	47.2 ± 4.2^a	48.4 ± 5.1^a	50.4 ± 5.6^b	<0.001
LVEDD index, mm/m^2	23.4 ± 2.5^a	24.3 ± 2.8^b	26.5 ± 3.2^c	<0.001
MMI, g/m^2	99.2 ± 21.9^a	106.6 ± 22.6^b	116.9 ± 24.1^c	<0.001
EF, %	47 ± 8.6^a	44 ± 8.5^b	38.7 ± 10.7^c	<0.001
Mitral annular calcification, n (%)	6 (7.1)	35 (9.1)	11 (11.2)	0.619

No-MR, no mitral regurgitation (MR) group; M-MR, mild MR group; M/S-MR group, moderate and severe MR group; LV EDD, left ventricular end-diastolic diameter; MMI, myocardial mass index; EF, ejection fraction. Difference is statistically significant between different letters (a, b, c), and insignificant between same letters.

3.6. *In-hospital outcomes*

In-hospital treatment duration did not differ significantly among the groups of MR, although a trend toward longer in-hospital stay was observed with increasing MR severity ($P = 0.05$) (Table 7). Severe heart failure or cardiogenic shock (Killip class 3 and 4) was more prevalent in M/S-MR group compared to no MR and M-MR groups ($P < 0.001$) (Table 7). Patients with no MR or mild MR were more likely to present in Killip class 1 compared to patients with moderate and severe MR ($P < 0.001$). There were more in-hospital cardiac death cases in M/S-MR group compared to patients with mild MR (8 [8.2%] vs. 6 [1.6%], respectively; $P = 0.002$). There were only 2 cases (2.4%) of in-hospital cardiac death in no MR group and difference from M-MR or M/S-MR group was not reported as statistically significant.

3.7. *Predictors of mitral regurgitation and its severity*

Predictors of MR after myocardial infarction in general MI ($n = 731$) and incidental MI populations ($n = 569$) were evaluated using logistic regression analysis. In univariate logistic regression analysis previous MI, female gender, atrial fibrillation, dyslipidemia, heart failure class 3/4 (Killip), RCA and LMS lesions were found to be related to development of MR in incidental MI and general MI populations (Table 8). Additional clinical parameters as peak CRP, extent of coronary artery disease have not shown additional predictive value in logistic regression models. Multivariate logistic regression analysis revealed that only age, EF, LVEDD index, and any form of atrial fibrillation are independent predictors of MR severity in acute MI ($P < 0.001$) (Table 9).

3.8. *Predictors of in-hospital death in acute MI population*

Heart failure class 3–4 (Killip), atrial fibrillation, and moderate and severe MR were predictors of in-hospital cardiac death in univariate regression analysis (Table 10). Due to relatively low overall incidence of fatal in-hospital outcomes (16 cases [2.8%] in first-ever MI population) multivariate regression analysis was not applicable to this study.

4. Discussion

Our study reports the incidence of hemodynamically significant (moderate and severe) functional (ischemic) mitral regurgitation of 17.2%. Reported incidence of significant (moderate and severe) MR after MI in previous large epidemiological studies ranges between 6% and 12% [3,7–9,11]. Majority of previous studies classified MR grade based on semi quantitative color flow Doppler mapping or angiographic criteria, while our study predominately employed quantitative echocardiographic Doppler parameters.

Population and community based cohort studies have identified various factors associated with MR in general population: female gender, advanced age, low BMI, renal dysfunction, prior myocardial infarction, arterial hypertension [12,13]. These and other clinical predictors of MR were as well explored in post-MI setting. Up to date there is uniform agreement on prognostic significance of age, female gender, LV dysfunction, dimensions and volumes in development of MR in post-MI setting [2]. Multiple other clinical factors were suggested to predict development of MR in acute coronary syndromes (ACS): concomitant comorbidities (diabetes, renal

Table 7 – In-hospital outcomes and distribution of heart failure classes according to Killip amongst MR groups.

	No-MR ($n = 85$)	M-MR ($n = 386$)	M/S-MR ($n = 98$)	P
In-hospital outcomes (% within MR groups)				
In-hospital treatment duration, days	8.4 ± 4.0	8.5 ± 5.5	9.9 ± 5.0	0.05
In-hospital death, n (%)	2 (2.4)^{a,b}	6 (1.6)^b	8 (8.2)^a	0.002
Killip heart failure class distribution (% within MR groups), n (%)				
I	19 (22.4)^a	72 (18.7)^a	5 (5.1)^b	<0.001
II	60 (70.6)^a	283 (73.3)^a	65 (66.3)^a	
III	4 (4.7)^a	16 (4.1)^a	16 (16.3)^b	
IV	2 (2.4)^a	15 (3.9)^a	12 (12.2)^b	

No-MR, no mitral regurgitation (MR) group; M-MR, mild MR group; M/S-MR group, moderate and severe MR group; HF, heart failure. Difference is statistically significant between different letters (a, b), and insignificant between same letters.

Table 8 – Univariate predictors of moderate and severe MR in acute MI populations.

Predictor	General population of myocardial infarction (n = 731)		Population of first myocardial infarction (n = 569)	
	OR (95% CI)	P	OR (95% CI)	P
Previous MI	2.0 (1.4–3.0)	<0.001	NA	NA
Age	1.1 (1.04–1.09)	<0.001	1.1 (1.02–1.07)	<0.001
Female gender	1.8 (1.2–2.6)	0.003	1.9 (1.2–2.9)	0.007
STEMI	0.7 (0.5–1.1)	0.1	0.7 (0.5–1.1)	0.16
AH	1.4 (0.8–2.6)	0.24	1.3 (0.7–2.5)	0.46
Obesity	0.8 (0.5–1.3)	0.44	0.6 (0.3–1.0)	0.07
Dyslipidemia	0.4 (0.3–0.7)	0.001	0.5 (0.3–0.9)	0.01
Diabetes	0.9 (0.6–1.5)	0.81	1.1 (0.6–2.0)	0.82
Killip class 3–4	5.0 (3.2–7.8)	<0.001	4.7 (2.7–8.1)	<0.001
MA calcinosis	1.6 (0.9–2.7)	0.1	1.3 (0.7–2.7)	0.43
Renal failure	2.5 (1.2–5.1)	0.01	2.2 (0.9–5.3)	0.07
Atrial fibrillation	2.7 (1.7–4.4)	<0.001	3.0 (1.7–5.2)	<0.001
LAD lesion	1.1 (0.7–1.7)	0.6	1.0 (0.6–1.6)	0.8
LCx lesion	1.6 (1.1–2.2)	0.02	1.4 (0.9–2.2)	0.11
RCA lesion	2.5 (1.6–3.8)	<0.001	2.6 (1.6–4.3)	<0.001
LMCA lesion	5.0 (2.4–10.3)	<0.001	5.8 (2.3–14.8)	<0.001

OR, odds ratio; MR, mitral regurgitation; NA, not applicable; STEMI, ST-segment elevation myocardial infarction; AH, arterial hypertension; MA, mitral annulus; LAD, left anterior descending artery; LCx, left circumflex artery; RCA, right coronary artery; LMCA, left main coronary artery.

failure), larger infarct zone, multivessel coronary artery disease (CAD) [10,12,14].

This study is in line with many of the previous findings. However, we have identified potentially new factors that may play a role in development of ischemic MR as inflammatory component (CRP rise) and disturbances of lipid profile which should be investigated separately in further studies.

Our study has shown that significant (moderate and severe) MR is more prevalent in the inferior MI group. Reports on whether the left ventricular (LV) infarction localization is a risk factor for MR severity differ: the incidence of ischemic MR has been reported to be higher in inferior compared to anterior MI localization [1,6,15]; however, the difference in incidence of moderate or severe MR based on MI localization was reported as insignificant by other author teams [3,12].

Table 9 – Multivariate predictors of moderate and severe MR in acute first MI population (n = 569).

Predictor	OR	95% CI	P value
Age	1.0	1.02–1.08	0.001
EF	1.0	0.93–0.99	0.008
LVEDD index	1.2	1.1–1.3	<0.001
AF	2.2	1.1–4.2	0.018
Gender	1.0	0.6–1.8	0.969
Number of affected CA	1.8	0.4–8.6	0.441
MA calcinosis	0.6	0.3–1.4	0.245
Q wave MI	0.9	0.5–1.7	0.792
STEMI	0.6	0.3–1.1	0.080
Dyslipidemia	0.8	0.4–1.6	0.477
Diabetes	0.9	0.4–1.9	0.801
AH	1.4	0.7–3.1	0.352
Renal failure	0.8	0.3–2.7	0.772
RCA lesion	1.2	0.3–6.2	0.788
LMCA lesion	1.5	0.3–6.7	0.611
LAD lesion	0.4	0.1–1.9	0.243
LCx lesion	0.7	0.1–3.2	0.596

OR, odds ratio; EF, ejection fraction; LV EDD, left ventricular end-diastolic diameter; AF, atrial fibrillation; CA, coronary arteries; MA, mitral annulus; MI, myocardial infarction; STEMI, ST-segment elevation myocardial infarction; AH, arterial hypertension; RCA, right coronary artery; LMCA, left main coronary artery; LAD, left anterior descending artery; LCx, left circumflex coronary artery.

Ischemic mitral regurgitation and functional mitral regurgitation in general terms share important associated clinical determinants (older age, female gender) [12,13]. It is reasonable to expect some overlap between these two clinical entities, however incidence and prevalence of significant MR is much higher in MI population or patients with prior MI, indicating important role of myocardial ischemia and LV remodeling [5,6]. Important role of LV remodeling is further supported by identifiable predictors of ischemic MR, confirmed and consistent with minor variations throughout the published studies and our results: extent of CAD, previous MI, larger LV dimensions and volumes, and decreased LV systolic function [2,3,11,12,15]. Significant MR is strongly associated with advanced age in MI and general population, therefore factors associated with ageing (varying degree of mitral annular calcification, long-standing arterial hypertension, comorbidities) need to be considered. Some of these clinical criteria have been previously addressed in the context of MR post MI (e.g. arterial hypertension, renal failure), and the results are diverging [16]. We have addressed the issue of mitral annular calcification (MAC), which is reported to be associated with ageing and MR [17]. Although in patients with MR MAC was reported relatively more often, the difference was not significant compared to patients with no MR, and MAC did not have any predictive value on development of significant (moderate and severe) MR in acute MI setting.

The relation of female gender to the presence of MR is reported in great extent [2]. Although female to male ratio was higher in moderate and severe MR group, our study has shown no impact of gender in predicting development of MR or in-hospital cardiac death when adjusted to other confounding factors.

Table 10 – Univariate predictors of lethal in-hospital outcomes.

Predictor	General population of myocardial infarction (n = 731)		Population of first myocardial infarction (n = 569)	
	OR (95% CI)	P	OR (95% CI)	P
Previous MI	1.8 (0.8–4.3)	0.19	NA	NA
Female gender	1.2 (0.5–2.8)	0.72	1.0 (0.4–3.0)	0.94
Killip class 3–4	30.2 (11.0–83.1)	<0.0001	20.3 (6.8–60.7)	<0.0001
Atrial fibrillation	3.1 (1.7–9.6)	0.002	4.8 (1.7–13.8)	0.003
Moderate/severe MR	5.1 (2.2–11.6)	0.0001	5.1 (1.9–14.1)	0.001
Mild MR	0.9 (0.2–4.5)	0.95	0.7 (0.1–3.3)	0.6

OR, odds ratio; MR, mitral regurgitation; MI, myocardial infarction; NA, not applicable.

Age, EF, LVEDDi, and atrial fibrillation (AF) were found to independently predict development of significant MR in multivariate regression analysis. Our study reports the prevalence of atrial fibrillation (AF) in incidental acute MI population of 11.8%, which corresponds to the reported rates of this arrhythmia in the literature [18]. However AF can be a causative or consecutive factor of either MI or MR, and preexistent silent AF is always a possibility. Any form of AF was found to be highly related to moderate and severe MR, and an independent predictor of significant MR in multivariate regression analysis.

Mitral regurgitation is reported to account for higher mortality rates in long-term follow-up [2]. Our study was aimed to assess and emphasize the impact of MR on short term (in-hospital) survival. Moderate and severe MR is strongly associated with in-hospital cardiac death, when considered separately from other clinical factors. Mild MR in acute in-hospital MI setting is not a significant prognostic factor of adverse events. This finding suggests the possibility of more important predictive role of mild MR to long-term follow-up outcomes, which is increasingly reported in the literature [3–5,8,11,12,18].

4.1. *Study limitations*

The major study limitation is the retrospective design, which disabled us from active control of clinical factors and outcome assessment, consequently adequacy of medical records was relied on. We acknowledge that selection bias may have affected the study cohort; however exclusion of cases as per applied criteria (unconfirmed MI, organic left sided heart valve disease or long-standing significant MR, inadequate echocardiographic imaging quality, etc.) was needed to prevent greater bias in identifying truly ischemic MR cases. Additionally, misclassification of study participants as the first incidental MI group was possible, as despite absence of previous history of ischemic heart disease, prior silent MI is a possibility in a proportion of patients with significant multivessel coronary artery disease. The latter limitation is applicable to all epidemiological studies of ischemic MR. Furthermore, inter-observer variability may account for misclassification of MR cases according to severity, however all echocardiographic scans are solely performed and reported by experienced cardiologists at HLUHS Kaunas Clinics and international guidelines are adhered to while grading valvular heart disease. Finally, retrospective study design precluded us from being able to assess the impact of timing factor from symptom onset to coronary artery reperfusion therapy in development of ischemic MR.

5. Conclusions

Functional mitral regurgitation in acute phase of myocardial infarction is prevalent. The major clinical associates are advanced age, atrial fibrillation, increased LV diastolic dimensions and lower EF. Moderate and severe, but not mild MR is an important clinical associate with in-hospital cardiac death.

Conflicts of interest statement

The authors report no conflict of interest in this study.

Acknowledgment

We are sincerely grateful to Kristina Jurėnienė for statistical advice.

REFERENCES

[1] Pant S, Neupane P, Pant OB, Paudel R, Kumar MP, Vijayashankar CS, et al. Mild functional ischemic mitral regurgitation following acute coronary syndrome: a retrospective study. Heart Views: Off J Gulf Heart Assoc 2011;12:93–8.

[2] Pellizzon GG, Grines LC, Cox AD, Stuckey T, Tcheng EJ, Garcia E, et al. Importance of mitral regurgitation in patients undergoing percutaneous coronary intervention for acute myocardial infarction: the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) trial. J Am Coll Cardiol 2004;43:1368–74.

[3] Bursi F, Enriquez-Sarano M, Nkomo VT, Jacobsen SJ, Weston SA, Meverden RA, et al. Heart failure and death after myocardial infarction in the community: the emerging role of mitral regurgitation. Circulation 2005;111:295–301.

[4] Barra S, Providencia R, Paiva L, Gomes PL, Seca L, Silva J, et al. Mitral regurgitation during a myocardial infarction – new predictors and prognostic significance at two years of follow-up. Acute Card Care 2012;14:27–33.

[5] Agricola E, D'Amato R, Stella S, Oppizzi M, Slavich M, Ancona BM, et al. Effects of mild ischemic mitral

regurgitation on ventricular remodeling and its contribution to congestive heart failure. J Am Soc Echocardiogr 2011;24:1376–82.
[6] Bahouth F, Mutlak D, Furman M, Musallam A, Hammerman H, Lessick J, et al. Relationship of functional mitral regurgitation to new-onset atrial fibrillation in acute myocardial infarction. Heart 2010;96:683–8.
[7] Singh JP, Evans JC, Levy D, Larson MG, Freed LA, Fuller DL, et al. Prevalence and clinical determinants of mitral, tricuspid, and aortic regurgitation (the Framingham heart study). Am J Cardiol 1999;83:897–902.
[8] Thygesen K, Alpert SJ, Jaffe SA, Simoons ML, Chaitman RB, White DH, et al. Third Universal definition of myocardial infarction. Eur Heart J 2012;33:2551–67.
[9] Jones CE, Devereux BR, Roman JM, Liu EJ, Fishman D, Lee TE, et al. Prevalence and correlates of mitral regurgitation in a population-based sample (The Strong Heart Study). Am J Cardiol 2001;87:298–304.
[10] Meris A, Amigoni M, Verma A, Thune JJ, Kober L, Valazquez E, et al. Mechanisms and predictors of mitral regurgitation after high-risk myocardial infarction. J Am Soc Echocardiogr 2012;25:535–42.
[11] Neskovic AN, Marinkovic J, Bojic M, Popovic AD. Early predictors of mitral regurgitation after acute myocardial infarction. Am J Cardiol 1999;84:329–32.
[12] Lamas AG, Mitchell FG, Flaker CG, Smith CS, Gersh JB, Basta L, et al. Clinical significance of mitral regurgitation after acute myocardial infarction. Circulation 1997; 96:827–33.
[13] Lancellotti P, Moura L, Pierard AL, Agricola E, Popescu AB, Tribouilloy C, 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;11:307–32.
[14] Chung SJ, Lin CF, Chua S, Fu M, Wu JC, Yip KH, et al. Clinical profile and outcome of first acute myocardial infarction with ischemic mitral regurgitation. Chang Gung Med J 2008;31:268–75.
[15] Chua S, Hung J, Chung YS, Lin CY, Fu M, Wu JC, et al. Primary percutaneous coronary intervention lowers the incidence of ischemic mitral regurgitation in patients with acute ST-elevated myocardial infarction. Circ J 2010;71:2386–92.
[16] Isla PL, Zamorano J, Quezada M, Almeria C, Rodrigo LJ, Serra V, et al. Prognostic significance of functional mitral regurgitation after a first non-ST-segment elevation acute coronary syndrome. Eur Heart J 2006;27:2655–60.
[17] Hong SJ, Kim SA, Hur J, Rhee SJ, Shim CY, Kim JS, et al. Mechanism of mitral regurgitation in the acute phase of inferior wall myocardial infarction – reduced closing force as a consequence of left ventricular systolic dysfunction in the presence of tethering as a determinant of mitral regurgitation. Circ J 2010;75:619–25.
[18] Yosefy C, Beeri R, Guerrero JL, Vaturi M, Scherrer-Crosbie M, Handschumacher MD, et al. Mitral regurgitation after anteroapical myocardial infarction: new mechanistic insights. Circulation 2011;123:1529–636.