Echocardiographic Assessment of Ischaemic Mitral Regurgitation, Mechanism, Severity, Impact on Treatment Strategy and Long Term Outcome

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ABSTRACT

Introduction: The commonest mitral regurgitation etiologies are degenerative (60%), rheumatic post-inflammatory, 12%) and functional (25%). Due to the large number of patients with acute MI, the incidence of ischaemic MR is also high. Ischaemic mitral regurgitation is a complex multifactorial disease that involves left ventricular geometry, the mitral annulus, and the valvular/subvalvular apparatus. Ischaemic mitral regurgitation is an important consequence of LV remodeling after myocardial infarction. Research Objectives: The objective of this study is to determine the role of echocardiography in detecting and assessment of mitral regurgitation mechanism, severity, impact on treatment strategy and long term outcome in patients with myocardial infarction during the follow up period of 5 years. Also one of objectives to determine if the absence or presence of ischaemic MR is associated with increased morbidity and mortality in patients with myocardial infarction. Patients and methods: The study covered 138 adult patients. All patients were subjected to echocardiography evaluation after acute myocardial infarction during the period of follow up for 5 years. The patients were examined on an ultrasound machine Philips IE 33 xMatrix, Philips HD 11 XE, and GE Vivid 7 equipped with all cardiologic probes for adults and multi-plan TEE probes. We evaluated mechanisms and severity of mitral regurgitation which includes the regurgitant volume (RV), effective regurgitant orifice area (EROA), the regurgitant fraction (RF), Jet/LA area, also we measured the of vena contracta width (VC width cm) for assessment of IMR severity, papillary muscles anatomy and displacement, LV systolic function ± dilatation, LV regional wall motion abnormality WMA, LV WMI, Left ventricle LV remodeling, impact on treatment strategy and long term mortality. Results: We analyzed and follow up 138 patients with previous (>16 days) Q-wave myocardial infarction by ECG who underwent TTE and TEE echocardiography for detection and assessment of ischaemic mitral regurgitation (IMR) with baseline age (62 ± 9), ejection fraction (EF 41±12%), the regurgitant volume (RV) were 42±21 mL/beat, and effective regurgitant orifice area (EROA) 20±16 mm², the regurgitant fraction (RF) were 48±10%, Jet/LA area 47±12%. Also we measured the of vena contracta width (VC width cm) 0.4±0.6 for assessment of IMR severity. During 5 years follow up, total mortality for patients with moderate/severe IMR–grade II-IV (54.2±1.8%) were higher than for those with mild IMR–grade I (30.4±2.9%) (P<0.05). After assessment of IMR and during follow up period 64 patients (46%) underwent CABG alone or combined CABG with mitral valve repair or replacement. In this study, the procedure of concomitant down-sized ring annuloplasty at the time if CABG surgery has a failure rate around 24% in terms of high late recurrence rate of IMR during the follow period especially after 18–42 months. Conclusion: The presence of ischaemic MR is associated with increased morbidity and mortality. Chronic IMR, an independent predictor of mortality with a reported survival of 40–60% at 5 years. Ischaemic mitral regurgitation has important prognosis implications in patients with coronary heart disease. Recognizing the mechanism of valve incompetence is an essential point for the surgical planning and a good result for the mitral repair. It is important that echocardiographers understand the complex nature of the condition. Despite remarkable progress in reparative surgery, further investigation is still necessary to find the best approach to treat ischaemic mitral regurgitation.

Key words: Ischaemic mitral regurgitation, Myocardial infarction, Ventricular remodelling, Regurgitant volume (RV), Effective regurgitant orifice area (EROA), Regurgitant fraction (RF), Papillary muscle displacement, Mitral annulus dilatation, Mitral leaflet tethering.

1. INTRODUCTION

The MV comprises two leaflets, annular attachment at the atroventricular junction, tendinous chords and the papillary muscles. Complete closure (coaptation) and correct apposition (symmetrical overlap, usually a minimum of 4-5mm) of both leaflets is essential.
in preventing regurgitation. The commonest mitral regurgitation etiologies are degenerative (60%), rheumatic (post-inflammation, 12%) and functional (25%). Due to the large number of patients with acute MI, the incidence of ischemic MR is also high. The secondary MR is not a primary valve disease but results from tethering (apical and lateral papillary muscle displacement, annular dilatation) and reduced closing forces, due to LV dysfunction (reduced contractility and/or LV dysynchrony). The diagnostic criteria of chronic IMR can be summarized as follows: MR occurring more than 16 days after myocardial infarction (MI) with one or more LV segmental wall motion abnormalities; significant coronary disease in a territory supplying the wall motion abnormalities and structurally normal MV leaflets and chordae tendineae. The third criterion is important to exclude patients with organic MR and associated CAD.

The underlying pathophysiologic mechanisms of IMR are often complex, resulting from several different structural changes involving left ventricular geometry, the mitral annulus, and the valvular/subvalvular apparatus. IMR occurs despite a structurally normal mitral valve as a consequence of a ventricular disease. Ischemic mitral regurgitation is a complex multifactorial disease that involves global and regional left ventricular remodeling as well as dysfunction and distortion of the components of the mitral valve including the chordae, annulus and leaflets. Ischemic MR affects patients’ prognosis, doubling mortality following myocardial infarction and heart failure.

In patients with ischemic mitral regurgitation after myocardial infarction, the mitral annulus enlargement is one of the determinants of the regurgitant volume and of the effective regurgitant orifice area. Echocardiographic diagnosis and assessment of ischemic mitral regurgitation are critical to gauge its adverse effects on prognosis and to attempt to tailor rational treatment strategy (Figure 1).

**Figure 1.** MR quantification by ratio of maximal distal jet area to left atrial area. Assessment of MR severity by distal jet area involves tracing the jet area (dashed white line) in the apical four chamber view and comparing the ratio of jet area to the left atrial area (solid white line).

### 2. RESEARCH OBJECTIVES

The objective of this study is to determine the role of echocardiography in detecting and assessment of mitral regurgitation mechanism, severity, impact on treatment strategy and long term outcome in patients with myocardial infarction during the follow up period of 5 years. Myocardial infarction was diagnosed based on medical history, hospital discharge documents, electrocardiography (ECG) and echocardiography findings. The evaluation of mitral regurgitation parameters and wall motion abnormalities of the left ventricle obtained by echocardiography (TTE and TEE) as a noninvasive diagnostic method. Also one of objectives to determine if the absence or presence of ischemic MR is associated with increased morbidity and mortality in patients with myocardial infarction.

### 3. PATIENTS AND METHODS

The study covered 138 adult patients. All patients were subjected to echocardiography evaluation after acute myocardial infarction during the period of follow up for 5 years. The echocardiography examinations were performed using commercially available equipment and standard techniques. The patients were examined on an ultrasound machine Philips iE 33 xMatrix, Philips HD 11 XE, and GE Vivid 7 equipped with all cardiologic probes for adults and multi-plan TEE probes. Examinations consisted of multiple tomographic planes including long-axis and short-axis views with color Doppler and continuous wave Doppler for detection and assessment of myocardial function and valvular disease. Degree and severity of MR was assessed semi quantitatively and quantitatively which includes the regurgitant volume (RV), effective regurgitant orifice area (EROA), the regurgitant fraction (RF), mitral regurgitation jet direction, Jet/LA area, also we measured the of vena contracta width (VC width cm) for assessment of IMR severity according to the ASE guidelines 2003 and ESC guidelines 2012.

Table 1 presents AHA Guidelines - however 2014 American College of Cardiology/American Heart Association guidelines propose a new classification scheme of valvular disease severity, based on a combination of echocardiographic and symptomatic parameters, with stages of “at risk” to “progressive” to “asymptomatic severe” to “symptomatic severe”, papillary muscles anatomy and displacement, annular dimension, LV systolic function ± dilation, LV regional wall motion abnormality WMA, LV WMI, Left ventricle LV remodeling, impact on treatment strategy and long term mortality.

| Parameter                  | Mild | Moderate | Severe |
|----------------------------|------|----------|--------|
| EROA-CIMR (cm²)            |      |          | < 0.2  |
| EROA-Primary MR (cm²)      |      | 0.2-0.39 | < 0.4  |
| VC width (cm)              |      | 0.3-0.69 | < 0.7  |
| Jet/LA area                |      |          | < 20%  |
| MR Reg. Volume             |      |          | 30-59 ml |

| Parameter                   | Mild | Moderate | Severe |
|-----------------------------|------|----------|--------|
| MR Reg. Volume              |      |          | < 30 ml |
| VC width (cm)               |      |          | 30-59 ml |

Table 1. Guidelines based reference ranges for grading MR–2003 ASE guidelines

### 4. RESULTS

We analyzed and follow up 138 patients with previous (>16 days) Q-wave myocardial infarction by ECG who underwent TTE and TEE echocardiography for detection and assessment of chronic ischemic mitral regurgitation (IMR). The demographic data, risk factors, clinical and comorbidity characteristics for all patients are shown on Table 2. The echocardiographic data and characteristics for all patients are shown on Table 3. The baseline age of patients was (62 ± 9), ejection fraction was (EF 35±14%), the regurgitant volume (RV) were 42±21 mL/beat, and effective regurgitant orifice area (EROA) 20±16 mm², the regurgitant fraction (RF) were 48±10%, Jet/LA area was 47±12%. Also we measured the of...
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vena contracta width (VC width cm) 0.48±0.6 for assessment of IMR severity. After assessment of IMR and during follow up period 64 patients (46%) underwent CABG alone or combined CABG with mitral valve repair or replacement.

During 5 years follow up, total mortality for patients with moderate/severe IMR–grade II-IV (54.2±1.8%) were higher than for those with mild IMR–grade I (30.4±2.9%) (P<0.05) (Figure 2) the total mortality for patients with EROA ≥20 mm² (54±1.9%) were higher than for those with EROA <20 mm² (27±2.7%) (P<0.05) (Figure 3), and the total mortality for patients with RVol ≥30 mL (56.8±1.7%) were higher than for those with RVol<30ml (29.4±2.9%) (P<0.05) (Figure 4).

In this study, the procedure of concomitant down-sized ring annuloplasty at the time if CABG surgery has a failure rate around 24% in terms of high late recurrence rate of IMR during the follow period especially after 18–42 months.

Also the study shows that revascularization alone does not result in a significant change in IMR grade both in patients with mild IMR or with moderate-to-severe IMR, it seems that the effects of revascularization on closing pressure are likely to depend on the presence and extent of viable myocardium. Also a significant percentage of patients with mild-to moderate IMR has an increase in degree or recurrence rate of IMR during the follow-up period of 5 years. The risk of operative mortality is higher after combined CABG and MV repair or replacement than after revascularization alone (7.5% -12% vs 2–5%).

Different drugs and combinations are usually used in patients with IMR in order to reduce the severity of MR and to reverse or delay the LV remodeling process. This study confirmed that the use of ACE-inhibitors and beta blockers in combination with diuretics is an independent predictor of better long-term survival in patients with IMR and LV dysfunction.

5. DISCUSSION

Mitral regurgitation can be primary due to leaflet abnormalities and secondary due to dysfunction of the left ventricle usually after myocardial infarction with structurally normal MV as ischaemic mitral regurgitation. The prevalence rate of development of mild or more severe degree of mitral regurgitation after myocardial infarction has been estimated to be up to 50% and is associated with worse prognosis (1-6), reviewed the prevalence of IMR after myocardial infarction, and reported that any IMR is present in 21% of patients, and 3–13%
have at least moderate IMR.

Ischaemic MR is not only a common but also a serious finding. The community based study of ischaemic MR among 30 day survivors of MI showed moderate or severe MR to be associated with a threefold increase in the risk of heart failure and increased risk of death at 5 year follow-up independent of age, gender, ejection fraction and Killip class (6). Mortality was increased even with mild MR (5).

Nesta et al (7) reported that anterior leaflet in the echocardiographic long axis view is convex toward the left atrium in normal subjects but is concave in patients with ischaemic MR, suggesting that the middle portion of the anterior leaflet is more tethered compared to the leaflet tip. Schwammenthal et al (10) have found that ischaemic MR dynamically changes in severity within a cardiac cycle, with the severity often maximal in early and late systole and minimal in mid-systole with maximal LV pressure. Hung et al (8) also confirmed such dynamic MR even in patients with surgical ring annuloplasty, confirming the importance of closing force.

The classic pattern of ischaemic MR involves a posterior wall motion abnormality with regional remodelling, leading to posterolateral and apical displacement of the (posterior) papillary muscle, the apical component of which appears to be the most important. This regional remodelling appears to be related to the regional scar burden (5). As the papillary muscle contributes chordae to both leaflets, the consequences are: (1) displacement of the posterior leaflet posteriorly; (2) development of a hockey stick deformity of the anterior leaflet due to tethered secondary chordae; and (3) displacement of the mitral coaptation point posteriorly (causing an asymmetric shape). The consequence is anterior leaflet override with a posterior MR jet (11).

The presence of moderate and severe MR appears to identify a higher risk group of patients who often progress early to congestive heart failure because of irreversible LV dysfunction and are at a higher risk for sudden death. This fact emphasizes the importance of MR as a marker of adverse outcome and suggests a cautious approach of such patients following AMI (12). MR seems to be a common finding after AMI. Previous large-scale trials, such as the SAVE study (Survival And Ventricular Enlargement), suggested that even mild MR is associated with high mortality after AMI (2). In addition, it has been well established that the presence of ischaemic MR is influenced by the size and location of the infarction. The presence of MR is associated with the presence of a larger LV diameter, indicating more extensive changes in LV geometry following AMI (13, 14, 4).

**Papillary muscle dysfunction**

The concept of PM dysfunction was based on clinical observations that ischaemic MR occurred after inferior myocardial infarction and secondary dysfunction of the medial PM (15). Historically, the mechanism of chronic IMR was attributed to papillary muscle dysfunction. However, further studies demonstrated that ischemia of papillary muscles themselves fail to produce significant MR without damage of the underlying myocardial wall. Papillary muscle discoordination—the papillary muscles are the main contributors to acute ischaemic MR. Although traditionally incriminated in chronic ischaemic MR, the importance of associated regional LV dysfunction has been recognized for nearly 40 years (11, 16). The investigators observed that addition of PM dysfunction with ischemia attenuated leaflet tethering and MR. This concept was later explored in clinical patients by Uemura et al (17). The data indicate that PM dysfunction is not the primary cause of ischaemic MR and that it may result in attenuated tethering and MR. These observations, rather than dis-
proving the tethering mechanism, actually confirm that the tethering distance from the PM tip to the mitral annulus is the final common pathway that determines the level of leaflet coaptation. Ischaemic MR was expected to result from leaflet prolapse due to the reduced longitudinal contraction of the PMs secondary to ischaemic dysfunction. Recent reports suggest the central role of tethering in ischaemic MR (18, 19).

Wall motion abnormalities are critically important in gauging local LV dysfunction in CIMR: the echocardiographer should identify and quantify wall motion as part of a comprehensive assessment of a global assessment of ischaemic burden. Indices of wall motion abnormalities underlying the posteromedial PM insertion are highly important in assessing CIMR (20). In patients with ischaemic mitral regurgitation after myocardial infarction, the mitral annulus enlargement is one of the determinants of the regurgitant volume and of the effective regurgitant orifice area. It seems that in the case of the mitral regurgitation with smaller regurgitant orifice area (<0.3 cm²), the importance of the regurgitation depends mainly on the enlargement of the annulus, on the other hand, in the case of the mitral regurgitation with larger regurgitant orifice area (>0.4 cm²) the leaflets restriction determined by the posterior papillary muscle displacement plays a very significant role (21). Measurement of vena contracta width may be a preferable means of assessing MR severity, although this is equally influenced by changes in LV pressure and dimensions. There is evidence that three dimensional echocardiography is superior to two dimensional techniques for the measurement of vena contracta, especially with eccentric jets (11, 22). Chronic IMR, an independent predictor of mortality with a reported survival of 40–60% at 5 years (5, 23, 24) is a progressive disorder in which MR-related LV volume overload promotes further LV remodelling, leading to worsened MR. Therefore, surgical correction, either by replacement or repair, is recommended for 3+ and 4+ IMR (25, 26).

The use of TEE intraoperatively and post-operatively in the evaluation of MR has been comprehensively reviewed by Sidebotham et al and Shakil et al (27, 28) TEE is important in assessment of patients undergoing surgical revascularization as it provides another opportunity to assess for CIMR. However, because of vasodilating effects of anesthesia, CIMR severity may be underestimated by intraoperative TEE.

It has clearly been demonstrated by Grigoni et al (5), that IMR aggravates prognosis after myocardial infarction corresponding with severity, and thus there is an absolute need for an effective treatment. Currently, the “gold-standard” treatment if IMR is concomitant down-sized ring annuloplasty at the time of CABG surgery. However, this procedure has a failure rate around 20–30% in terms of recurrent IMR after the first 2 - 4 years, and there are few, if any, other disciplines in cardiac surgery where we consider such a result a “gold standard”. This underscores that we still have not identified a truly effective and lasting treatment if IMR, that relieves patient suffering and improves survival. Therefore, IMR is very much an unsolved challenge (29-31).

Several studies had demonstrated that revascularization alone does not result in a significant change in IMR grade both in patients with mild-to-moderate IMR (1+ or 2+) and with moderate-to-severe IMR (3+ or 4+) and a significant percentage of patients with mild-to-moderate IMR has an increase in degree or recurrence of IMR during follow-up (25, 29–35). However, revascularization alone appears to produce long-term survival similar to that for revascularization plus annuloplasty both in patients with moderate and severe IMR, whereas the risk of operative mortality is higher after combined revascularization and MV repair than after revascularization alone (9.5%-15% vs 3-5%). Kim et al (33) reported a 5-year actuarial survival in patients with 3+or4+IMR of 44%+5% after combined procedure and 41%-77% after revascularization alone. Wong et al (34) reported no significant difference in mortality for concomitant annuloplasty compared with revascularization alone in patients with 3+IMR with a 5-year survival of 67.5% in the whole group of patients (36). Whereas good results have been reported by Bax et al (37) - high late recurrence rates of MR after ring annuloplasty have been published McGee et al (24) reported a 28% recurrence rate of 3+ or 4+MR at 6 months. Furthermore, Serry et al (38) reported a recurrence rate of 36% for 2+MR and 20% for 3+to 4+MR at 28 months, while Tahta et al (39) reported a recurrence rate for 2+ to 4+MR of 29% at 35 months.

Myocardial revascularization does not necessarily reverse ischaemic MR. In a study of coronary bypass surgery in 136 patients with moderate ischaemic MR, half showed an improvement in MR, but resolution of MR occurred in only 9%, and 40% had residual moderate or severe MR (25). The effects of revascularization on closing pressure are likely to depend on the presence and extent of viable myocardium. The mechanisms responsible for recurrence of CIMR after surgical revascularization and restrictive annuloplasty remain elusive. In some instances, the mechanism is ongoing adverse LV dilatation and spherical remodelling that worsens tethering (40, 41). The current medical therapy for heart failure includes vasodilators (ACE-inhibitors), diuretics and beta blockers, and its beneficial effects on symptoms of heart failure in patients with IMR and LV dysfunction may be dramatic.

Various combinations of these drugs are commonly used in these patients for two reasons: to reduce the severity of MR and to reverse or delay the LV remodeling process. The use of afterload-reducing agents, including ACE-inhibitors, might reduce the regurgitant volume and improve forward output by decreasing the pressure gradient between LV and left atrium. Vasodilators may effectively decrease regurgitant flow through the effect of systolic unloading on the regurgitant orifice area (3, 7). A similar effect of reduction in MR is obtained with preload reduction through the use of diuretics that decrease ventricular size and further reduce tethering with a consequent decrease in the regurgitant volume (3). The use of ACE-inhibitors and b-blockers is an independent predictor of better long-term survival in patients with IMR and LV dysfunction, as reported by Wu and colleagues (42). This could be due to the effects of ACE-inhibitors and b-blockers on progression of LV remodeling and prevention of sudden death (35).

6. CONCLUSION

The ischaemic mitral regurgitation has many specific features which differentiates it from organic regurgitations. The clinical signs of MR and its severity are unreliable in ischaemic MR. Ischaemic mitral regurgitation has important
prognosis implications in patients with coronary heart disease. It should not be underestimated and this underlines the need for a complete evaluation but should be interpreted specifically, in particular as regards quantification of the regurgitation. Recognizing the mechanism of valve incompetence is an essential point for the surgical planning and for a good result of the mitral repair. In the patient’s candidates to surgery, the role of the echocardiographic exam is to identify the mechanisms of valve regurgitation and to quantify it. The excess mortality, which was considerable for ERO ≥ 20 mm² and RVol ≥ 30 mL, suggests that quantification of MR in the post-MI chronic phase is essential for risk stratification. Furthermore, the high risk associated with IMR suggests that such patients should be managed actively and that all therapeutic options of medical and surgical treatment should be considered promptly. Even today, we have no reliable predictors of recurrent and persistent mitral regurgitation.

The presence of ischaemic MR is associated with increased morbidity and mortality. Chronic IMR, an independent predictor of mortality with a reported survival of 40–60% after 5 years, is a progressive disorder in which MR-related LV volume overload promotes further LV remodeling, leading to worsened MR. It is important that echocardiographers understand the complex nature of the condition. Despite remarkable progress in reparative surgery, further investigation is still necessary to find the best approach to treat ischaemic mitral regurgitation.

**Conflict of interest:** None declared.

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