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Comparisons between the Outcome of Mitral Repair versus Replacement in Patients with Ischemic Heart Disease with Severe Ischemic Mitral Regurgitation and Undergoing Coronary Artery Bypass Grafting (CABG) Surgery: Review Article

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ABSTRACT
Ischemic mitral regurgitation (IMR) is a complication that frequently happens following myocardial infarction (MI). Around fifty percent of cases develop IMR following MI, and more than ten percent of them have moderate or severe IMR. A poor prognosis is predicted by the presence of IMR. Previous research has demonstrated a higher severity of IMR related to a shorter long-term survival. The mortality rate of cases with even mild IMR is 17% higher than that of those without it. The most effective operation for moderate ischemic mitral regurgitation with concomitant coronary Artery Disease (CAD) is also a topic of controversy. In retrospective research, we investigated the real-world operational results of cases having CAD and ischemic mitral regurgitation who underwent mitral valve surgeries and concomitant coronary artery bypass grafting. An elevated surgical mortality rate and poor long-standing survival are related to the ischemic mitral regurgitation operational management.
Keywords: IMR, mitral valve repair, cardiopulmonary bypass

INTRODUCTION

Leaflet tethering, papillary muscle displacement, decreased closing forces, as well as annular dilatation are the primary mechanisms of IMR that are linked to left ventricular remodelling following MI. Consequently, it is an aspect of functional mitral regurgitation. For a prolonged duration, IMR management was a topic of debate. The absence of robust evidence and clinical data is the cause of this controversy. A recently published practice guideline defines severe ischemic mitral regurgitation as a class I indication for operational management. Nevertheless, the appropriate surgical modality, whether it be repair or replacement, is still being investigated [(1)].

Presently, the most frequently conducted operation for treating cases with severe IMR is restrictive mitral valve annuloplasty. Nevertheless, the technique has been related to a ten to twenty percent incidence of persistent MR in the first few months following the procedure and a fifty to seventy percent incidence of recurrent mitral regurgitation at 5 years. Additionally, the presence of persistent or recurrent mitral regurgitation is related to a greater prevalence of cardiac events and a lower survival rate. Mild systemic hypothermia (32ºC), cardiopulmonary bypass (CPB), and antegrade crystalloid cardioplegia were utilized through all procedures, which were conducted through midline sternotomy. The decision to carry out replacement or repair was left to the individual surgeon. A concomitant coronary bypass operation has been carried out on primary coronary vessels or branches that showed luminal stenosis of over seventy percent on a preoperative coronary angiogram [(2)].

This work aimed to compare between the results of mitral valve replacement Vs. repair among cases with IMR undergoing revascularization.

Coronary Artery Disease (CAD)
Introduction

CAD is a disorder defined as an inadequate oxygen and blood supply to the myocardium. The oxygen supply-demand imbalance is the consequence of the coronary arteries blockage. It regularly includes plaques development in the coronary arteries lumen, that block blood flow. It's the primary reason for fatality within the United States and all over the world. It was an unusual reason for mortality at the turn of the 20th century. Fatalities resulting from coronary artery disease reached their peak in the middle-1960s and subsequently decreased. Nevertheless, it remains the most prevalent reason for mortality globally[(3)].

Etiology

Coronary artery disease is a multifactorial phenomenon. Etiologic factors may be generally divided into modifiable and non-modifiable factors. Age, genetics, family history and gender are all non-modifiable factors. Obesity, smoking, psychosocial variables, and lipid levels are all modifiable risk factors. Males are more susceptible compared to females. Hypercholesterolemia continues to be a significant modifiable risk factor for CAD. Elevated levels of low-density lipoproteins (LDL) elevated CAD risk, although elevated levels of high-density lipoproteins (HDL) decreased CAD incidence [(4)].

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Epidemiology

CAD is prevalent in developing as well as developed countries. In 1 research, it has been calculated that coronary artery disease accounted for 2.2 percent of the disease burden globally and 32.7 percent of cardiovascular diseases. Despite gender, the prevalence of CAD is found to increase with age. The CAD incidence in the 45 to 65 age group in the ONACI registry in France was approximately one percent. It elevated to approximately four percent as the age group reached the age of 75 to 84 [5].

Pathophysiology

The atherosclerotic plaque development is a mark of the coronary artery disease pathophysiology. Plaque is a fatty accumulation that restricts a vessel lumen and blocks blood flow. The initial phase of the process involves the development of a "fatty streak". Foam cells, which are also known as lipid-laden macrophages, are responsible for the formation of fatty streaks through subendothelial deposition. Eventually, this plaque might develop in size or become stable if no more insult happens to the endothelium. The lesion will become calcified gradually, and a fibrous cap will form if it becomes stable [5].

History and Physical Examination

A detailed history and physical examination are crucial for identifying coronary artery disease, which can progress into stable ischemic heart disease or ACS, and must be assessed for chest pain, dyspnea, and physical activity. The physical investigation must involve palpation, inspection, and auscultation to detect jugular venous distention, peripheral edema, and acute distress, with fluid thrill and heave being evaluated [6].

Evaluation

The primary modalities for evaluating coronary artery disease are Echo, EKG, CXR, cardiac catheterization, stress test, and blood work. [3]

Electrocardiogram (EKG)

An EKG is a vital test for assessing CAD, measuring electrical activity in the cardiac conduction system utilizing 12 leads. It provides information on heart physiology, anatomy, and pathologic processes, and is cost-effective and user-friendly. [3]

Echocardiography

Echocardiography is a non-invasive heart ultrasound used in acute and chronic settings to detect heart conditions, diagnose pulmonary pathologies, assess therapy response, and perform stress testing in outpatient settings, but may be more expensive than EKG. [4]

Stress Test

It is a non-invasive method in assessing CAD, especially within cases of suspected angina. It involves artificial heart stress exposure, and aborts if abnormalities occur. [3]

Chest X-ray

The chest X-ray is a crucial tool for assessing cardiac disease, with standard images including left lateral decubitus and standing posteroanterior. Anteroposterior projection is sometimes attained, but interpretation is limited. Valuable information regarding the heart, lungs, and vasculature can be obtained through the proper analysis of PA and AP views, but should be done stepwise. [4]

Blood Work

Blood work is essential for diagnosing and evaluating therapeutic reactions within various conditions, using B-type natriuretic peptides, cardiac enzymes, complete blood counts, metabolic panels, lipid panels, and liver function tests for acute and chronic conditions. [3]

Cardiac Catheterization

Cardiac catheterization is the most reliable method for assessing ischemic coronary heart disease, but can cause complications and allergic reactions in non-ACS settings[4]

Differential Diagnosis

CAD has a broad-spectrum differential diagnosis due to its proximity to other organs. Acute chest pain can mimic various conditions, while stable ischemic heart illness can also be similar to peptic ulcer illness, pleuritis, and GERD. Careful history, diagnostic studies, and physical investigation are essential for accurate diagnosis. [3]

Side Effect Management

Surgical and medical treatment of ischemic heart disease involves side effects and complications, which can be lessened through physician expertise, careful selection, and case education, including bleeding, idiosyncratic reactions, and myalgias. Beta-blockers, ACEIs, PCIs, and CABGs can cause various complications, including bradycardia, hypotension, in-stent restenosis, and stent thrombosis. CABG may also lead to cardiac tamponade, arrhythmias, infection, post-op hemorrhage, phrenic nerve damage, and kidney dysfunction [7].

Ischemic Mitral Regurgitation Prognosis

The prognosis is influenced through various factors including patient's gender, age, ethnicity, family history, medication compliance, dietary habits, healthcare accessibility, financial status, and the number of arteries involved. Comorbid disorders like hypertension, diabetes, chronic kidney disease, and dyslipidemia also impact the outcome [8].

Complications of MI

Coronary artery disease is generally related to the following complications: acute coronary syndrome, arrhythmias, mitral regurgitation, congestive heart failure, pericarditis, aneurysm formation, ventricular free wall rupture, and mural thrombi. [1]

Ischemic mitral regurgitation (IMR)

Introduction

IMR is a secondary MR complication of ischemic heart illness, resulting from primary or functional valvular involvement. Secondary IMR is caused by an imbalance in the closing and tethering forces, which happens when valve leaflets and chordae are structurally regular, while primary IMR happens following an acute myocardial infarction [9].

Prevalence

In Europe, MR, the 2nd most frequent valve disease, impacts thirty-one percent of the people. Ischemic mitral regurgitation, the 2nd cause, accounts for 25% of patients. The ischemic mitral regurgitation prevalence has raised, with 17-40% of AMI patients showing early echocardiographic or clinical evidence [10].

IMR Mechanisms

Chronic IMR is primarily caused by type IIIb valvular dysfunction, with leaflet motility restricted in systole, more common within cases with prior inferior AMI. Ischemic mitral regurgitation is less commonly resulting from fibrosis and prolongation of the PM (type II). Apical and posterior PM displacement identify mitral tenting. While most cases show remote infarction and ventricular remodeling, acute ischemia with irregularities in regional wall motion may result in leaflet tethering [11] (Fig. 1).

The mitral ring's saddle-shape is crucial for maintaining leaflet stress, but loss or crushing due to LV remodeling can lead to increased stress in secondary mitral MR. Adverse ventricular remodeling after an AMI causes tension in the cords, restricting leaflet movement and reducing mitral valve closing force. Secondary MR is dynamic and reliant on load conditions and cardiac cycle phase [9].

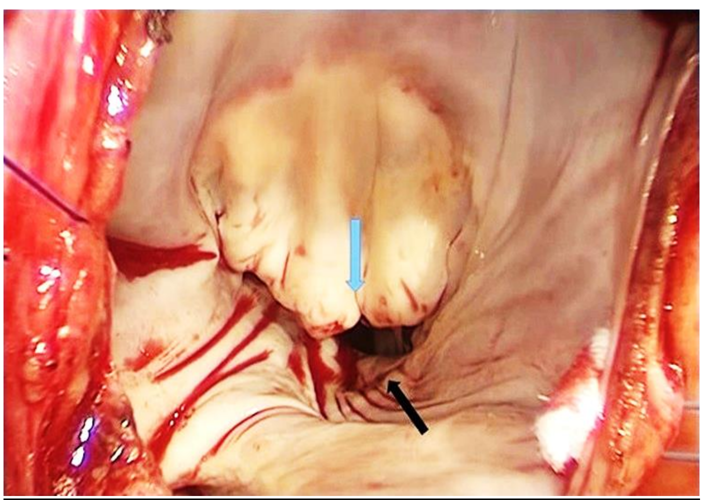

Fig. 1: A surgical image of an ischemic mitral valve from the left atrium demonstrating the anterior leaflet (blue arrow) and the posterior leaflet tethering (black arrow) [12].

Ischemic Mitral Regurgitation Echocardiographic Assessment

Echocardiography is used to identify MV irregularities (leaflets, mitral annulus, sub valvular apparatus, and/or left ventricle) which result in valvular regurgitation [9]

Ventricular remodeling and deformation of the mitral system

Echocardiography is used to determine LV diameters, 2D biplane volumes, and sphericity index. It helps in the determination of segmental alterations, parietal thinning, posterior and apical displacement of the anterior and posterior papillary muscles, mitral apparatus deformation, coaptation distance, ring size, tenting area, and leaflets angles. 3D echocardiography offers advantages over 2D in assessing tenting volume [9].

Morphology of the MV

The MV's morphology reveals an asymmetric closure pattern, with a "hockey stick" sign on the echocardiogram. Coaptation changes are the result of the anterior leaflet being situated below the posterior leaflet. An eccentric jet of inadequacy is observed ipsilateral to the posterior leaflet, indicating an inferolateral or inferior infarction. [11]

Ischemic mitral regurgitation recurrence predictors following repair

Recurrence rates of ischemic mitral regurgitation are thirty percent following surgical repair at three years, and they increase to approximately seventy percent at five years. The negative remodeling of the LV is perpetuated by the presence of residual mitral regurgitation following operation, leading to raised tethering of the mitral leaflets. This vicious cycle eventually leads to an increase in the severity of MR. A worse prognosis is correlated with the presence of significant postoperative IMR compared to its absence [13].

TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography.

Local and global remodeling of the left ventricle;

Valve tethering.

MR recurrence is primarily due to leaflet tethering, with aneurysm/dyskinesia being a significant predictor. Restrictive LV filling indicates advanced myocardial dysfunction, leading to negative remodeling post-repair. Severe dilatation reduces the likelihood of reverse remodeling, resulting in worse long-term outcomes. Transthoracic echocardiography (TTE) predicts failed mitral repair in patients with a coaptation distance of 1 centimeter or higher, tenting area of 2.5-centimeter square, and a coaptation angle of 45 degrees or higher. Recurrence is also predicted by an angle among the anterior leaflet tip and the mitral ring. Preoperative transesophageal echocardiography (TOE) can predict long-term surgical failure in severe MR patients with a ring diameter of 37 mm, tenting area of 1.6 cm^2, and severe MR, with TOE-3D offering comprehensive visualization of MV system components [14] (Fig. 2).

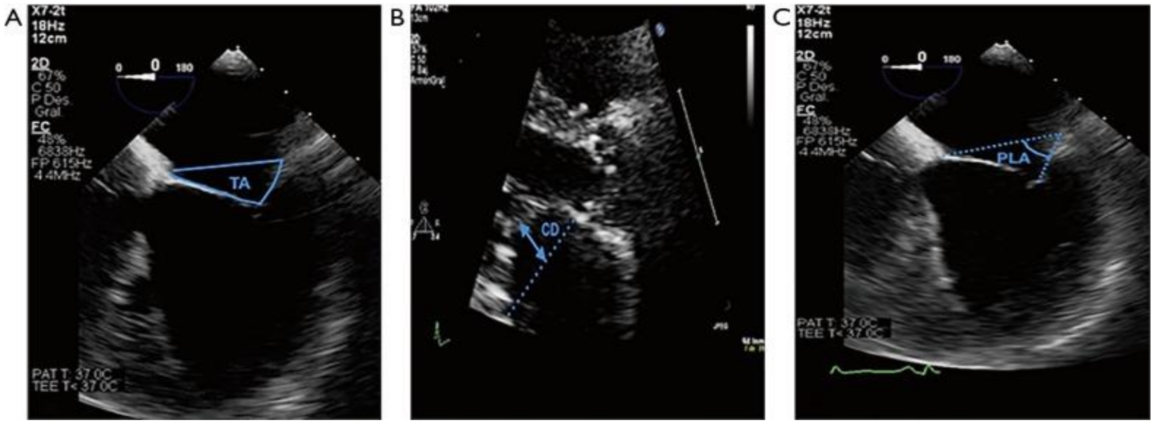

Fig. 2: Echocardiographic evaluation of mitral valve deformation. (A) Tenting area (TA); (B) coaptation distance (CD); (C) posterior leaflet angle (13).

Ischemic mitral regurgitation severity quantification

Transthoracic echocardiography is a highly effective technique for evaluating the mechanism and severity of IMR, despite having certain limitations. The subsequent echocardiographic techniques are utilized to evaluate the extent of mitral regurgitation [9].

Color flow imaging

Color flow imaging is a commonly utilized method for evaluating IMR, assuming that the regurgitation severity increases the extension and size of the jet in the larynx. Nevertheless, this method is inaccurate due to technical and hemodynamic factors, leading to underestimation and overestimation [15].

Vena contracta (VC) width

Vena contracta width is the width of the inadequacy jet following covering the regurgitant orifice. It's measured in 2 perpendicular projections to the line of commissures. Mild MR is indicated by a VC of less than 3 mm, while severe MR is defined by a VC of 7 mm or greater. In IMR, regurgitant orifice is more extended along coaptation line. Doppler image orientation isn't suitable for a precise cross-sectional view of the vena contracta. An average eight-millimeter vena contracta diameter is reported as severe MR. Intermediate vena contracta values (three to seven millimeters) require quantitative validation. The evaluation of VC through 3-dimensional echocardiography is still under study [16].

Doppler volumetric technique: The Doppler volumetric technique utilized to calculate the MR volume when VC and PISA aren't precise. It involves calculating the variance among total and systemic stroke volume. However, this technique is time-consuming and can be inaccurate in cases of significant aortic regurgitation, making it not recommended for first-line quantification [17].

The flow convergence technique: The flow convergence technique is the most suggested quantifiable method in determining PISA in gastrointestinal reflux (MR) conditions, involving four-chamber apical view, ultrasound beam alignment, gain adjustment, depth reduction, and Doppler measurements. [9]

Anterograde velocity of mitral inflow

A peak velocity E greater than 1.5 m/s is indicative of severe mitral stenosis, but a dominant A wave excludes it in cases older than fifty. The TVI ratio, which is a strong parameter for evaluating the extent of MR, is the ratio among mitral inflow Doppler and aortic flow [18].

Pulmonary venous flow

The S-wave velocity in pulmonary vein flow increases through severe MR severity, a sensitive nevertheless non-specific parameter that affects ventricular dysfunction, atrial fibrillation, and elevated left atrium pressure. In severe forms, this effect may reverse [18].

Continuous wave Doppler of mitral regurgitation jet

Severe mitral regurgitation is determined through the continuous jet Doppler MR signal intensity, which is dashed, triangular, dense, and has an early peak speed. This suggests an obvious regurgitant pressure wave or increased LA pressure as a result of severe MR. The intensity is challenging for recording in eccentric MR; however, the continuous jet Doppler mitral regurgitation is a qualitative parameter. [9]

Exercise stress echocardiography (ESE)

Exercise stress echocardiography has the potential to assess symptoms, rule out or confirm ischemic causes, assess myocardial viability, and detect symptoms and subclinical ischemic ventricular disfunction in asymptomatic ischemic mitral regurgitation cases. It has prognostic value, as increased EROA with exercise increases morbidity, mortality, and cardiac events [19].

Strain echocardiography

The use of tissue Doppler, speckle tracking, and ventricular deformation in evaluating valvular disorders is still being investigated. Longitudinal strain can detect subclinical LVSD, while traditional 2D-echocardiography techniques may overlook ventricular function deterioration in severe chronic MR patients. Although speckle tracking analysis is superior to tissue Doppler and traditional left ventricle systolic function analysis, its application has been restricted through limitations of various echocardiographic systems [20] (Fig. 3).

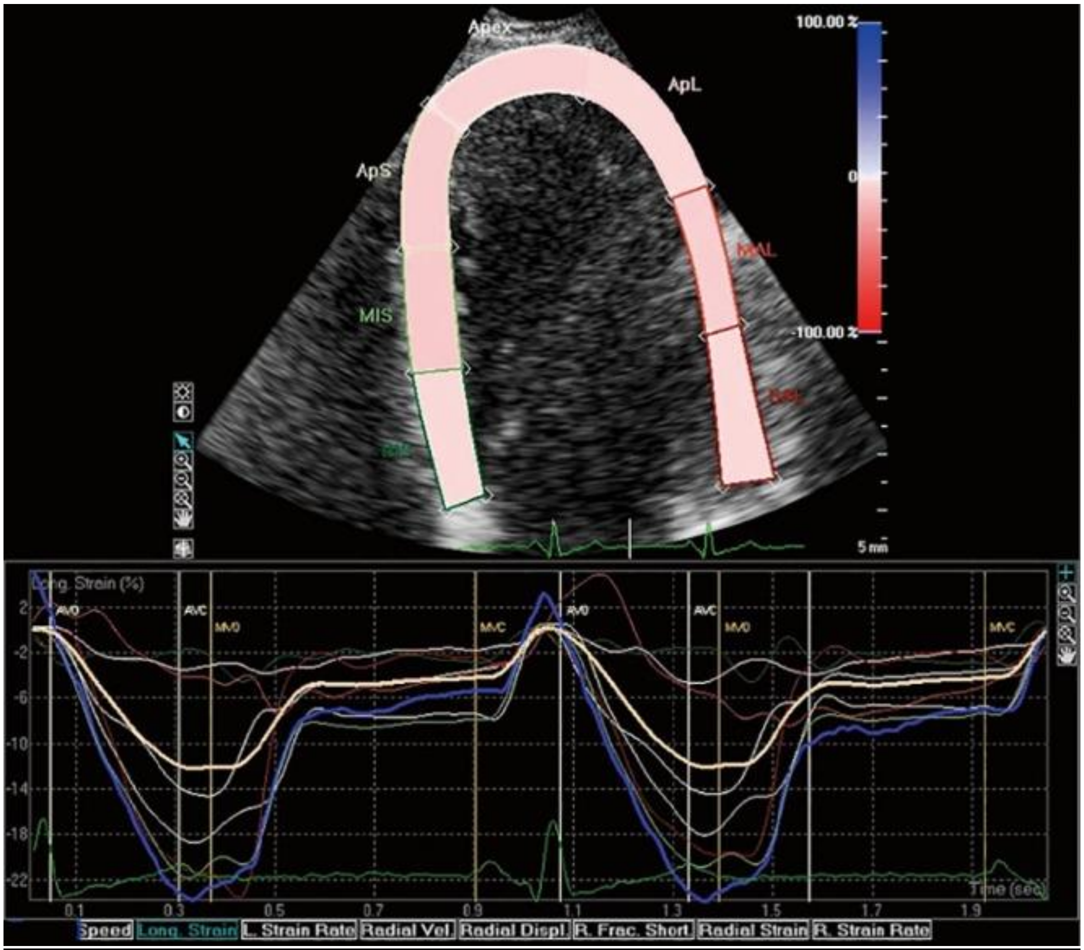

Fig. 3: Left ventricular longitudinal strain determination and an apical 4-chamber view of a transthoracic echocardiography utilizing speckle tracking imaging. TTE, transthoracic echocardiography [12].

TOE: two and three-dimensional

TOE is a highly effective alternative to TTE imaging when it isn't suitable for the characterization of valvular cardiac disease and the development of an operative strategy. When assessing a case with MR of ischemic origin, TOE is beneficial in excluding organic etiology. Additionally, the transducer's near to the valve, the sub valvular apparatus, and the regurgitation jet, that is directed at it, results in high-quality images [21] (Fig. 4).

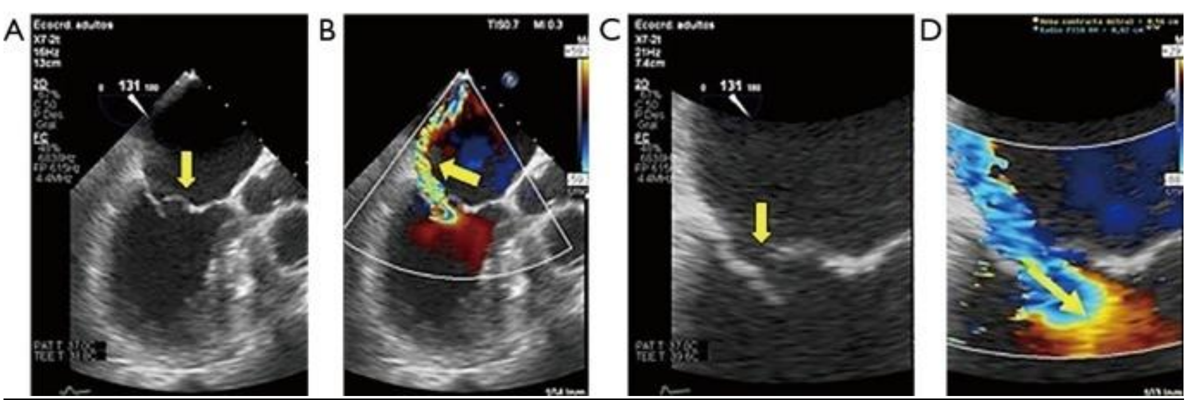

Fig. 4: Transesophageal echocardiography, or TOE enables a more precise quantifying tenting area, traction, mitral ring, and reduction in the apposition surface. (A) Reduction in the apposition surface (yellow arrow); (B) Coanda impact in IMR (yellow arrow); (C) Transesophageal echocardiography zoom-mode of the mitral valve with a reduction in mitral valve apposition surface (yellow arrow); (D) proximal isovelocity surface area and mesosystolic area (yellow arrow) [21].

Cardiovascular magnetic resonance in IMR

Magnetic resonance imaging (CMR) aids in cardiac pathology study, but its evaluation is limited when echocardiography doesn't confirm MR diagnosis due to lower resolution and morphoanatomical evaluation. CMR can quantify contractility, ventricular volumes, viability, and myocardial thickness through late enhancement pattern analysis with gadolinium, detect ischemia, analyze contractile reserve, and study extracellular volume using complex techniques [22].

Prognosis

Survival and progression of post-AMI heart failure are significantly influenced by IMR. A higher mortality rate correlates to its presence in comparison to cases who don't develop MR, which is directly correlated to its severity. Survival is predicted to be forty percent in moderate-severe ischemic mitral regurgitation, sixty-two percent within mild, and 84 percent within cases with no ischemic mitral regurgitation, depending on the severity. EROA ≥20 mm^2 indicates a lower rate of survival at five years compared to with no mitral regurgitation (38%±5% vs. 61%±6%, P<0.001), despite function of the ventricular [22].

Treatment

Medical treatment

Acute ischemic mitral regurgitation has a significant hemodynamic effect and could need surgical intervention. Despite the fact that this is correlated with greater mortality compared to scheduled operation in chronic cases, the risk of mortality increases if it isn't managed intensively. Aldosterone antagonists and angiotensin-converting enzyme inhibitors (ACEI) were used to improve functional MR in degenerative MR, but there are few studies on IMR. Captopril improves functional MR due to idiopathic dilated cardiomyopathy, while beta-blockers prevent ventricular remodeling and improve ejection fraction [23].

Cardiac resynchronization therapy (CRT)

Prior to heart transplantation within LVSD cases, cardiac rehabilitation therapy is recommended for cases having secondary myocardial infarction (MR) and LVSD who are candidates for electronic device treatment. CRT can enhance symptoms, life quality, and mitral regurgitation severity. Nevertheless, mitral regurgitation following cardiac resynchronization therapy implantation may have a worse prolonged prognosis. A current study demonstrated a decline in mitral regurgitation severity and enhanced PM alignment and left ventricle systolic function within cases having inferoposterior scars [24].

Coronary Revascularization and MV Replacement Vs. Repair for Ischemic Mitral Regurgitation

Indication

The operational indications for ischemic mitral regurgitation are unclear, but clinical guidelines generally recommend mitral intervention for severe MR, symptomatic patients, and optimal medical treatment. ESC/EACTS guidelines classify MV surgery as a class I recommendation for CABG. [20]

Moderate ischemic mitral insufficiency

Moderate intraventricular remodeling (IMR) within cases undergoing CABG is a controversial topic. Recent meta-analyses show a higher incidence of ischemic mitral regurgitation within the isolated coronary artery bypass grafting group, but this doesn’t affect severe negative impacts, mortality, ventricular remodeling, or functional ability. These researches have restrictions, including not including patients with sub-valvular apparatus repair techniques with no adjusting the traction forces and the ventricular geometry on the mitral leaflets. Currently, surgeons make decisions based on symptoms and additional risks of adding procedures to CABG. Future studies could improve evidence by proposing an algorithm that facilitates operative decisions by utilizing a mathematical model that defines the MV biomechanics and its components [20].

MV Repair Vs. Replacement

The surgical therapy for ischemic mitral regurgitation that is most efficient is also the most controversial. Although some authors observed a decrease in fatality with MV repair comparing with replacement, others didn't notice any significant variances. Researches show a rise in IMR relapse with MV repair, but this doesn't usually worsen functional status or quality of life. The American Association for Thoracic Surgery Guidelines provide guidance based on predictors of IMR recurrence. Studies on MV replacement Vs. repair frequently don't involve sub-valve repair methods, that might reduce ischemic mitral regurgitation recurrence rates and state new operational indications [25].

Myocardial revascularization

Myocardial revascularization is a procedure for correcting IMR by restoring valve function and normalizing ventricular geometry. However, it is insufficient in many cases and significantly improves postoperative IMR [25].

MV replacement

The mitral valve replacement evolution, a therapy for mitral valve disorders, has been facilitated by the advancements in surgical reconstruction. It is now advised to maintain both mitral leaflets, reduce the left ventricular size and post-load, and enhance systolic function and ventricular remodeling. Large valves may block ventricular dynamics and conduction, so it is recommended to oversize the prosthesis. The type of mechanical prosthesis is related to enhanced hemodynamics and functional capacity during exercise [26].

Reconstructive operation

Reconstructive operation for mitral valve repair in ischemic mitral regurgitation started with restrictive annuloplasty, which uses a ring smaller than the intertrigonal distance. Rigid and complete rings provide a more durable repair. Leaflet coaptation must be 8 mm or more and residual MR by TOE must not exceed 1/4. However, this technique doesn't adjust other insufficiency mechanisms, like PM displacement, traction on leaflets, and LV remodeling. New surgical alternatives have emerged with similar mortality rates, better traction management, better remodeling processes, and lower IMR recurrence. [20]

PM sling

Hvass *et al*.**[27]** suggested that the 2 PMs be approximated by a group surrounding them .In the medium term, this method leads to a decrease in moderate or higher repeated MR, fewer traction on mitral leaflets, and better reverse remodeling of the left ventricle in comparison with isolated annuloplasty.

Papillary muscles (PM) replacement

This procedure involves the use of a Gore-Tex suture to connect the head of each papillary muscles to the ipsilateral mitral ring. 1 or 2 of these rings may be relocated. To ensure that the MV maintains its diastolic opening, it is essential to act on both heads of the posterior muscle and to reposition the muscle in the direction of the anterior ring [26]**.**

A rise in the leaflet's surface area

This method, that may be applied to any of the mitral leaflets, is designed to decrease traction and rise the curvature of the leaflets. An incision is made near the base of the corresponding leaflet, parallel to the mitral annulus, to create an opening that is utilized to position a pericardial patch. This is the method utilized to achieve this. Outcomes that are favorable in the short and medium term were documented [28] (Fig. 5).

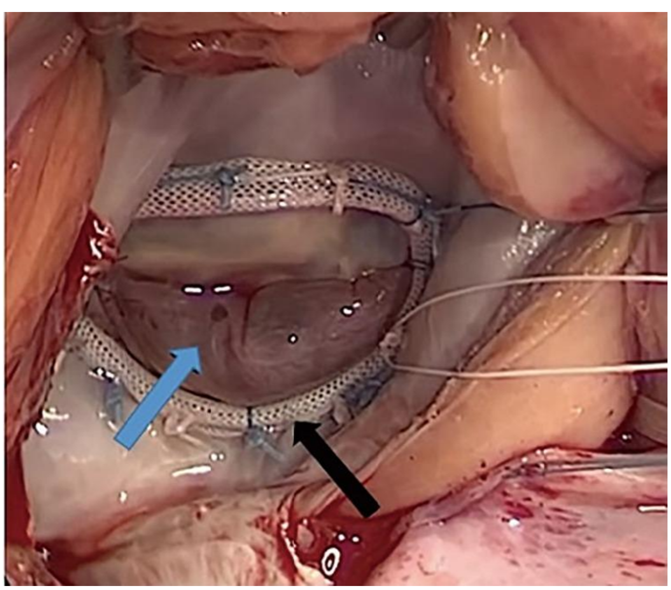

Fig. 5: Surgical image of a true-sized annuloplasty (black arrow) and an ischemic mitral valve repair with posterior leaflet augmentation using a pericardial patch (blue arrow) [12]

The Coapsys device

The Coapsys device, a left trans-ventricular cord which is installed beneath the ventricular wall, changes the left ventricle morphology in response to stress, thereby reducing IMR and enhancing NYHA functional class. The RESTOR-MV trial has demonstrated increased survival and reduced adverse effects, while reducing stress on myofibrils, potentially contributing to long-term left ventricle remodeling [29].

Ring-loop-string plastic

Bothe has recently proposed a repair technique that entails the suturing of a PTFE loop at the base of the anterolateral papillary muscle. This is followed by the placement of advanced PTFE sutures with one end fixed to the posteromedial papillary muscle base and the other at the left atrium, crossing the mitral valve at the level of P2. Future research is required to illustrate its medium- and long-term effectiveness [30]**.**

Transcatheter MV therapies

Left ventricle systolic dysfunction incidence is linked to great mortality in 2ry mitral regurgitation and medical treatments, prompting the search for less invasive techniques. Over a decade, trials have evaluated the effectiveness and safety of edge-to-edge transcatheter techniques, with the 1st trial showing promising results but not establishing inclusion criteria based on MR etiology. The EVEREST II trial established promising outcomes in cases with functional NYHA, left ventricle size, and life quality improvement after transcatheter therapies and surgery. However, Transcatheter therapies necessitated a 4:1 need for operative reoperation, and the surgical group experienced a greater incidence of complications. Nevertheless, the most current Surgery Thoracic Score records indicate that both treatment groups require reoperation [30]

Ethical considerations: All the procedures of the research were approved by the Cardiothoracic Surgery Department and the Investigation Ethics Committee of Faculty of Medicine, Suez Canal University. Administrative consents required were taken. This study was performed in compliance with the Declaration of Helsinki, the code of ethics of the World Medical Association.

DECLARATIONS

- **Funding:** No fund
- **Availability of data and material:** Available
- **Conflicts of interest:** No conflicts of interest.
- **Competing interests:** None

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