STUDY PROTOCOL

TMRSM_R

Transient Mitral Regurgitation Following Septal Myectomy: A Retrospective Echocardiographic Study

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List of Abbreviations/ Terminology *(in alphabetical order)*

Abbreviation	Name
HOCM	Hypertrophic Obstructive Cardiomyopathy
LVOT	Left Ventricular Outflow Tract
LV	Left Ventricle
MR	Mitral Regurgitation
MV	Mitral Valve
PMVL	Posterior Mitral Valve Leaflet
SAM	Systolic Anterior Motion
TEE	Transesophageal Echocardiography
TTE	Transthoracic Echocardiography

Protocol Summary

Full Title	Transient Mitral Regurgitation following Septal Myectomy A Retrospective Echocardiographic Study
Short Title	TMRSM_R
Sample Size	N= 150
Study Population	All patients who underwent septal myectomy at Toronto General Hospital between January 1, 2022 and December 31, 2025
Study Design	Retrospective Observational Cohort Study
Study Data Period	1-January-2022 to 31-December-2025
Study Primary Objectives	To determine the proportion of patients with ≥ moderate MR on intraoperative post-bypass TEE that improves to ≤ mild MR on predischarge transthoracic echocardiography (TTE).
Date of Protocol	12-May-2026
Protocol Version	1.0

1.0 General Information

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2.0 Background Information

Hypertrophic obstructive cardiomyopathy (HOCM) is characterized by asymmetric septal hypertrophy and dynamic LVOT obstruction. Septal myectomy is the standard surgical therapy for symptomatic patients refractory to medical management.

Mitral regurgitation (MR) in HOCM is classically related to systolic anterior motion (SAM) of the anterior leaflet. Following myectomy, relief of LVOT obstruction typically reduces SAM-associated MR. However; intraoperative transesophageal echocardiography (TEE) frequently demonstrates persistent or new MR following separation from cardiopulmonary bypass.

Clinical observation suggests that a subset of this MR may be due to transient posterior leaflet restriction, potentially related to incomplete myocardial protection in hypertrophied myocardium. This may result in MR that resolves prior to discharge without requiring mitral valve intervention. Misinterpretation of this transient phenomenon may lead to unnecessary surgical procedures.

There is currently limited systematic evaluation of the mechanism and natural history of MR observed immediately following myectomy. This study aims to address this knowledge gap using retrospective echocardiographic review.

3.0 Study Objectives and Hypothesis

Primary Objective
To determine the proportion of patients with ≥ moderate MR on intraoperative post-bypass TEE that improves to ≤ mild MR on predischarge transthoracic echocardiography (TTE).

Secondary Objectives

a) To characterize the echocardiographic mechanism of MR, with emphasis on posterior leaflet restriction.
b) To evaluate interobserver agreement between two independent reviewers.
c) To identify clinical and operative predictors of persistent MR at discharge.
d) To assess the relationship between intraoperative MR severity and postoperative MR.

4.0 Study Design

This is a retrospective observational cohort study.

5.0 Selection of Subjects

Inclusion Criteria

- Adult patients (≥18 years)
- Undergoing septal myectomy for HOCM
- Availability of intraoperative post-cardiopulmonary bypass TEE images
- Availability of predischarge TTE

Exclusion Criteria

- Concomitant primary mitral valve disease due to structural abnormalities, prior ischemic MR or previous MV intervention (repair or replacement)
- Inadequate echocardiographic image quality precluding MR assessment
- Patients without paired TEE and TTE studies

6.0 Study Procedure:

Echocardiographic Analysis
Two independent reviewers with expertise in perioperative echocardiography will assess all imaging studies. Reviewers will be blinded to each other's assessments and to clinical outcomes.

Intraoperative TEE (Post-Bypass)
MR severity (graded using integrative criteria consistent with ASE guidelines)

Mechanism of MR:

- Posterior leaflet restriction
- Residual SAM
- Iatrogenic MR (direct surgical injury of chorda, incision of the abnormal papillary muscle)
- Mixed or alternative mechanisms
- Leaflet motion (Carpentier classification)
- LV systolic function and regional wall motion abnormalities, especially at inferior and posterior walls

Predischarge TTE

- MR severity (same grading framework)
- LV systolic function
- Residual LVOT gradient

Discrepancies between reviewers will be resolved by consensus or third adjudication if required.

Clinical and Operative Data Collection

- Age
- Sex
- Preoperative MR severity
- Preoperative LV mass
- Severity of preoperative coronary artery disease (% occlusion)
- Septal thickness
- Cardiopulmonary bypass time
- Aortic cross-clamp time
- Myocardial protection strategy (where available)
- Postoperative hemodynamic support

7.0 Risks/Benefits

Risks: This is a minimal risk study.
We do not contact participants. No interventions will be done. We only collect data retrospectively. Data will be de-identified.
Benefits: There are no direct benefits to participants. However, the knowledge gained from this research study may contribute to a better understanding of intraoperative and postoperative TEE in patients with mitral regurgitation (May improve intraoperative echocardiographic interpretation, may help to reduce unnecessary valve interactions, inform myocardial protection strategies in HOCM surgeries)

8.0 Statistics

8.1 For Statistical Analysis:

- Using descriptive statistics for baseline characteristics,
- Paired comparison of MR severity (TEE vs TTE)
- Using non parametric testing, interobserver agreement was assessed
- Using Cohen’s Kappa coefficient
- Multivariable logistic regression for identify predictors of persistent MR

8.2 Sample size:

As this is a retrospective study, all eligible cases will be included. Approximately 150 cases are expected. About 35–40 surgeries are performed annually at Toronto General Hospital. Data will be collected on transient mitral regurgitation following septal myectomy over three years (2021–2025), with an expected sample size of 150 cases.

9.0 Data abstraction, Storing, Handling and Direct Access to Source Data/Documents:

Data will be obtained from the institutional myectomy database, Syngo echocardiography archival and reporting systems and EPIC electronic medical records.
Data are entered into a secure departmental database on institutional hardware.
All records are de-identified and stored in accordance with institutional policy.

Only the study master log will contain direct identifiers, and it will be stored separately in a password-protected database.
Access is provided only to the study team.
Study data will be retained in a secure database for 10 years after completion the study and then data will be securely deleted/destroyed.

10.0 Ethics:

10.1 Ethical/Regulatory Framework

This study will be conducted in accordance with the ethical principles laid down in the Declaration of Helsinki. The study will be conducted in compliance with the protocol, GCP guidelines, and applicable regulatory requirements.

10.2 Patient information and waiver of Consent

We will identify patients eligible for inclusion in the study by screening the cardiac surgical schedule from a to-be-determined date, where 150 consecutive eligible septal myectomy surgical patients will be identified.

This research involves no or minimal risk to subjects. A waiver of informed consent would not adversely affect the rights and welfare of the subjects. To limit bias (selection bias) in which patients are included in the study, our goal is to collect data from 150 consecutive septal myectomy patients at Toronto General Hospital.

This research would not be able to be practically carried out without a waiver of informed consent. The risk to patient privacy is reasonable in relation to the importance of the knowledge to be gained. Additionally, only de-identified data will be collected from patient charts and analyzed in aggregate. No individual patient data will ever be presented or published

11.0 Publication Policy:

The results will be submitted for presentation at national and international cardiovascular anesthesia, echocardiography, and cardiac surgery meetings. The investigators intend to submit the completed study for publication in JCVA

13.0 References:

1. Ommen SR, Mital S, Burke MA, et al. 2020 AHA/ACC Guideline for the Diagnosis and Treatment of Patients With Hypertrophic Cardiomyopathy. Circulation. 2020;142:e558-e631. The guideline specifically recommends intraoperative TEE during septal myectomy to assess mitral valve anatomy/function and adequacy of myectomy.
2. Zoghbi WA, Adams D, Bonow RO, et al. Recommendations for Noninvasive Evaluation of Native Valvular Regurgitation. J Am Soc Echocardiogr. 2017;30:303-371.
3. Ayati A, et al. Comparing long-term outcomes of septal myectomy and mitral valve replacement in hypertrophic obstructive cardiomyopathy. J Card Surg / related open-access report. 2024. Isolated myectomy may correct HCM-related MR, with mitral valve replacement reserved for intrinsic valve disease.
4. Walter EMD, et al. Long-term outcome of simultaneous septal myectomy and anterior mitral leaflet retention plasty in HOCM. Ann Cardiothorac Surg. 2017 Jul;6(4):343.doi:10.21037/acs.2017.03.08.