Heart Valve Society Mitral Tricuspid Valve Database Project

Project Application

Center: Leiden University Medical Center, Albinusdreef 2, 2333 ZA Leiden, The Netherlands

Name: *Meindert Palmen, MD, PhD, Nina Ajmone Marsan, MD, PhD, Anton Tomšič, MD, PhD, Bart JA Mertens (MD, PhD), Robert J.M. Klautz, MD, PhD*

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Title of the project application: The Effect of Post-repair Mitral Valve Geometry and Function on the Incidence of Recurrent Mitral Regurgitation

Centers can enroll patients with mitral and/or tricuspid valve disease consecutively or apply project based. This project application form should be completed and submitted to the Scientific Committee for approval. However, it is highly recommended that centers contribute as much data as possible to achieve the study objectives, facilitate the extraction of their own outcomes, and increase their access in the application for multi-center analysis.

Introduction

Mitral valve repair is the gold standard of treatment for patients suffering from severe primary mitral regurgitation (MR). The intraoperative goal is to preserve or restore full leaflet motion, create a large surface of coaptation and remodel and stabilize the annulus [1]. Although nowadays almost all mitral valves can be repaired with zero or trace residual MR on intraoperative transoesophageal echocardiography (TOE), during follow-up some patients will develop recurrent MR (rMR), despite the presence of a good initial repair [2]. From literature, we know that coaptation length may influence valve repair durability. This geometric parameter is strongly inversely correlated to the incidence of rMR [3-5]. However, little is known on other valve-related parameters that may influence repair durability.

Aim of the project

Our aim is to identify qualitative and quantitative intraoperative postrepair TOE parameters associated with future rMR.

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Included patients

The following inclusion criteria will be applied:

1) Adult patients (18+ years)
2) Surgical mitral valve repair for primary (organic) degenerative mitral valve disease
3) Postoperative rMR

The following exclusion criteria will be applied:

1) Diagnosis of secondary (functional) mitral valve disease
2) Diagnosis of other types of mitral valve disease causing mitral valve insufficiency (including active or healed mitral valve endocarditis, rheumatic heart disease, and ischemic mitral regurgitation)
3) Patients with concomitant aortic valve replacement
4) Patients with degenerative disease without mitral valve prolapse as the primary mechanism of mitral regurgitation (e.g. central regurgitant mitral valve caused by degenerative mitral annular calcification)

Duration project

☑ **Retrospective** □ Prospective

Inclusion period 2010 - 2024

Follow-up period 2010 – 2024

Study design and Methods

A retrospective nested case-control study (NCC) will be performed to analyze patients who underwent surgical mitral valve repair for primary (degenerative) mitral valve disease. Patients who did develop postoperative rMR are considered as cases and will be matched at the follow-up time-point where rMR occurred (the case index date) to patients free of rMR at that same time-of-follow-up. These latter matched patients will be regarded as the matched controls. Cases will be matched 1:2 to controls.

The cases (patients who developed rMR during follow-up) are identified retrospectively from the centers that are participating in this study (noted below).

The control group (patients who did not develop rMR during follow-up) is comprised of a retrospective cohort from the LUMC. Because of the low rMR rate seen in high-volume centers, we expect that it would be possible to select a control group of at least twice the size of the case group. However, if the control group does not prove to be large enough (because of the matching), then cases will be matched to controls 1:1 or control patients from other centers could be used.

Cases are matched to controls on the case index dates, based on the following characteristics at the index date:

- Follow-up duration
- Age
- Gender
- Valve pathology (e.g. P2 prolapse)

The intraoperative postrepair TOE marks the starting point for the follow-up. For the patients who developed rMR, the date of this event defines the (case) index date, at which point of follow-up suitable patients are matched free from rMR at that index date. Matching criteria are defined at the index date. Matched patients share the same index date and must be alive (at risk) at the index date.

If a patient postoperatively developed endocarditis with resulting MR, the date of this event will mark the end of follow-up for that case. For matched control patients, the end of follow-up is defined as time to the (corresponding) case index date.

Primary outcome
Significant (≥ grade 2+) rMR during early-, mid-, and long-term postoperative follow-up identified by follow-up TTE/TOE.

Addendum
Changes in mitral valve geometry include changes in any of the parameters mentioned and illustrated below in 'Quantitative measures in systole' and **Appendix 2**.

Collection of data outside standard of care
Data collection for this study consists of measurements derived from intraoperative TOE and routine follow-up TTE taken periodically after the index cardiac surgery for all patients. This could be yearly or every 2 years, depending on the follow-up protocols of the participating centers. Additionally, for patients with rMR, the TTE taken at the moment of the MR recurrence is added to the data collection. All echocardiograms are performed and collected within standard of care. However, most of the echocardiographic measurements are not routinely performed, and thus they should be newly measured for the study. The measurements are as follows:

Intraoperative pre- and post-repair TOE for all patients:

1) Qualitative:
    a. Grade of MR prerepair and grade of MR postrepair based on the recommended multiparametric approach [6]
        i. Mild
        ii. Moderate
        iii. Moderate-severe
        iv. Severe
    b. Jet direction of MR prerepair/jet direction of MR postrepair
        i. Central
        ii. Eccentric

   c. Mobility posterior leaflet (qualitatively assessed)
      i. Normal
      ii. Reduced
      iii. Absent
2) Quantitative measures in systole:
   a. Anterior MV leaflet projection in the annular plane (mm)
   b. Posterior MV leaflet projection in the annular plane (mm)
   c. Coaptation position (ratio between a. and b.)
   d. Coaptation depth (mm)
   e. Coaptation length (mm)
   f. Posterior mitral valve leaflet angle (°)
   g. Tenting area (cm^2)
   h. Intercommissural distance (mm)
3) Quantitative measures diastole:
   a. Anterior MV leaflet length (mm)
   b. Posterior MV leaflet length (mm)
4) Quantitative left ventricular measurements:
   a. LVEF (%)
   b. LVEDD (mm)
   c. LVESV (mL)
   d. LVEDV (mL)

MV: mitral valve; LVEF: left ventricular ejection fraction; LVEDD: left ventricular end diastolic diameter; LVESV: left ventricular end systolic volume; LVEDV: left ventricular end diastolic volume.

Follow-up TTE:

1) Qualitative in patients with rMR:
   a. Grade of rMR based on recommended multiparametric approach
      i. Mild
      ii. Moderate
      iii. Moderate-severe
      iv. Severe
   b. Jet direction rMR
      i. Central
      ii. Eccentric
   c. Mechanism of rMR
      i. Carpentier Type I: normal leaflet motion
      ii. Carpentier Type II: excessive leaflet motion
      iii. Carpentier Type IIIa: restricted leaflet opening
      iv. Carpentier Type IIIb: restricted leaflet closure
      v. Post MV repair endocarditis

2) Quantitative measures in systole in all patients:
    a. Anterior MV leaflet projection in the annular plane (mm)
    b. Posterior MV leaflet projection in the annular plane (mm)
    c. Coaptation position (ratio between a. and b.)
    d. Coaptation depth (mm)
    e. Coaptation length (mm)
    f. Posterior mitral valve leaflet angle (°)
    g. Tenting area (cm^2)
    h. Intercommissural distance (mm)
3) Quantitative measures diastole in all patients:
    a. Anterior MV leaflet length (mm)
    b. Posterior MV leaflet length (mm)
4) Quantitative left ventricular measurements in all patients:
    a. LVEF (%)
    b. LVEDD (mm)
    c. LVESV (mL)
    d. LVEDV (mL)

Please refer to the **Appendix 2** for the indexed schematic representations of the intraoperative TOE MV measurements.

Intraoperative TOE measurements should be performed after MV repair at 120-160 degrees mid-esophageal to obtain a long axis view for optimal assessment of the MV. The 60-70 degrees mid-esophageal commissural view should be used to measure the intercommissural distance. The posterior MV leaflet (PMVL) angle will be measured during systole by measuring the angle between the MV plane and the plane corresponding to the line between the posterior part of the annuloplasty ring and posterior leaflet free edge as depicted in the **Appendix 2**. In some cases, the MV cannot be clearly assessed from this angle, in which a 80-100 degrees mid-esophageal 2 chamber view, or a 0-20 degrees mid-esophageal 4 chamber view can be used instead to assess the mitral valve. Note, however, that the PMVL is not always visible during echocardiographic assessment due to a shadow cast by the annuloplasty.

Moreover, few surgical data which are not described in the HVS Data Dictionary should be collected from the operative report. They include the following:

1) MV leaflet repair approach
    a. Resection
    b. Neochordae
2) Repaired leaflet segments (multiple options possible)
    a. A1
    b. A2
    c. A3
    d. P1

   e. P2
   f. P3
3) Ring type
   a. Memo 3D
   b. Memo 4D
   c. Simulus semi-rigid ring
   d. Sovering
   e. Physio ring
   f. Physio II ring
   g. CG future
   h. Cosgrove annuloplasty band
   i. other
4) Ring size
   a. 26mm
   b. 28mm
   c. 30mm
   d. 32mm
   e. 34mm
   f. 36mm
   g. 38mm
5) Indentation closure
   a. Yes
   b. No
6) Commissural closure
   a. Yes
   b. No
7) Type of annuloplasty device used
   a. Full ring
   b. Partial band

Variables entered

All other variables of interest from the data dictionary can be found in the data dictionary **Appendix 1** attached to this application.

Details relating to the aortic valve or the tricuspid valve and details relating to mental health are not of interest for this study.

Data analysis plan

Intraoperative postrepair geometry measurements are presented as means and standard deviation (SD) for normally distributed data or medians and interquartile range (IQR) when not normally distributed. To assess geometric differences between the rMR (case) group and the non-rMR

(control) group, mixed models will be applied as required for comparison, to take the matched design into account.

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In order to identify which intraoperative TOE measurements are associated with rMR, time-to-event data is analyzed using univariable and multivariable conditional logistic regression. Mitral valve geometric measurements derived from postrepair intraoperative TOE are entered into the model as continuous variables to assess the association between postrepair intraoperative TOE measurements and rMR. Furthermore, EUROSCORE II will be added into the model. Multivariate model building may make use of prioritised a-priori rankings of potential risk factors, which take collinearity into account. Significant (≥ MR2+) rMR is the event of interest in this study. To assess for the presence of violations in model assumptions, residuals should be plotted versus fitted values and investigated graphically. In multivariable models, the Bonferroni correction for multiple testing is used to calculate respective P-values. Variables entered into the model should be collected from the intraoperative postrepair Trans-Oesophageal Echocardiography (TOE). We will investigate if age is not associated with euroscore II

Anticipated Participating centers

1) Leiden University Medical Center
2) San Raffaele University Hospital (Milan)
3) Universitätsspital Zürich
4) Hosptital Clinico de Barcelona (Barcelona)
5) Universiteit Ziekenhuis Leuven
6) Frankfurt University Hospital
7) Augsburg University Hospital
8) Other centers willing to participate in this project

References

1. Carpentier A. Cardiac valve surgery--the "French correction". J Thorac Cardiovasc Surg. 1983 Sep;86(3):323-37
2. Flameng W, Herijgers P, Bogaerts K. Recurrence of mitral valve regurgitation after mitral valve repair in degenerative valve disease. Circulation. 2003 Apr 1;107(12):1609-13.
3. Sasaki H et al. Short Coaptation Length is a Predictor of Recurrent Mitral Regurgitation After Mitral Valve Plasty. Heart Lung Circ. 2021 Sep;30(9):1414-1421.
4. Hage Fet al. Coaptation length predicts early- and intermediate-term durability following degenerative mitral repair. Eur J Cardiothorac Surg. 2022 Aug 3;62(3):ezac194.
5. Uchimuro T et al. Post-repair coaptation length and durability of mitral valve repair for posterior mitral valve prolapse. Gen Thorac Cardiovasc Surg. 2014 Apr;62(4):221-7.
6. Lancellotti P, Pibarot P, Chambers J, La Canna G, Pepi M, Dulgheru R, Dweck M, Delgado V, Garbi M, Vannan MA, Montaigne D, Badano L, Maurovich-Horvat P, Pontone G, Vahanian A,

Donal E, Cosyns B; Scientific Document Committee of the European Association of Cardiovascular Imaging. Multi-modality imaging assessment of native valvular regurgitation: an EACVI and ESC council of valvular heart disease position paper. Eur Heart J Cardiovasc Imaging. 2022 Apr 18;23(5):e171-e232.

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Appendix 1: Variables of interest from the data dictionary.

	Variable ID	DEFINITION
Preoperative: Demographic factors	Year of _Birth	Year of birth
	Sex	Sex
	Gender	The patient's gender identity
	heightvalue	The height of a person measured in meters (m)
	weightvalue	The body weight of a person measured in kilogram preoperatively (kg)
	Anticoagulants	Anticoagulants being taken preoperatively
	CPS	Critical preoperative state based on the Euro Score II definition
	PulmHT	Pulmonary pressure preoperative in mmHg
	Dialysis	Please indicate if the patient is under any dialysis treatment preoperatively
	Myocardialinfarction	Indicate whether the patient has a documented history of myocardial infarction preoperatively
	PriorCardiacProcedure	Please indicate if the patient has undergone cardiac procedure preoperatively (before the index valve repair)
	Diabetesmellitus	indicate if the patient has a documented history of diabetes mellitus regardless of duration of disease or need for anti-diabetic agents preoperatively
	ChronicLungDis	indicate whether the patient has a documented history of chronic lung disease preoperatively
	NYHA	Objective assessment of NYHA class (I-IV) preoperatively
	Prior_Endocarditis	Please indicate whether the patient has ever been diagnosed with endocarditis or has active endocarditis preoperatively. Endocarditis is diagnosed according to the modified duke criteria (reference). Active is defined as still under antibiotic treatment at the time of procedure
	CreatinineValue	Serum creatinine value in mg/dL preoperatively
	LVEF	Left ventricular ejection fraction (%) preoperatively
Intraoperative: valvular measurements and operative characteristics	LVD1	Please indicate the dimensions of the left ventricular end systolic diameter in mm intraoperatively
	LVD2	Please indicate the dimensions of the left ventricular end diastolic diameter in mm intraoperatively
	LVD3	Please indicate the dimensions of the intraventricular septum diameter in mm intraoperatively
	MVregurg	Please indicate which grade of regurgitation is present
	MechMVRegurg	Please indicate which mechanism of the mitral valve regurgitation (Carpentier classification)
	MVLesion	Please indicate the location of the leaflet prolapse

	MVDiseaseEtiology	Please indicate which disease etiology has been defined
	TreatmentDate	Date of index surgery
	ACC	Cross clamp time in minutes (min)
	CPB	Cardiopulmonary bypass time in minutes (min)
	SurgeryAccess	Please indicate which surgical access site was used
	ProcedureTime	Procedure time in minutes (min)
	ConcomitantQx	Please indicate if the patient had concomitant surgery
	MVrepairType	Please indicate the type of mitral valve repair
Postoperative: clinical outcomes	Deceaseddate	in case a patient has deceased during follow up: the date of death of the person
	ValveMort	(yes/no) Valve-related mortality is any death caused by structural valve deterioration, nonstructural dysfunction, valve thrombosis, embolism, valve-related bleeding, or prosthetic valve endocarditis; death related to reintervention on the operated valve
	BaselineRhythm	Baseline rhythm of the patient at time of measurement. If a patient has a permanent/temporary pacemaker, but has AF/sinus on electrocardiogram, AF/sinus should be coded
	BleedingEvent	If bleeding event occurs during follow-up, please indicate the date of this event
	Endocarditis	If the patient develops endocarditis during follow-up, please indicate the date of this event
	ValveThromb	If valve thrombosis occurs during follow-up, please indicate the date of this event
	strokeEvent	If stroke occurs during follow-up, please indicate the date of this event
	Re-intervention	If a patient is undergoing a reintervention for the mitral valve please indicate the date
	HeartFailure	In case of unplanned hospital admission for heart failure: please indicate the date

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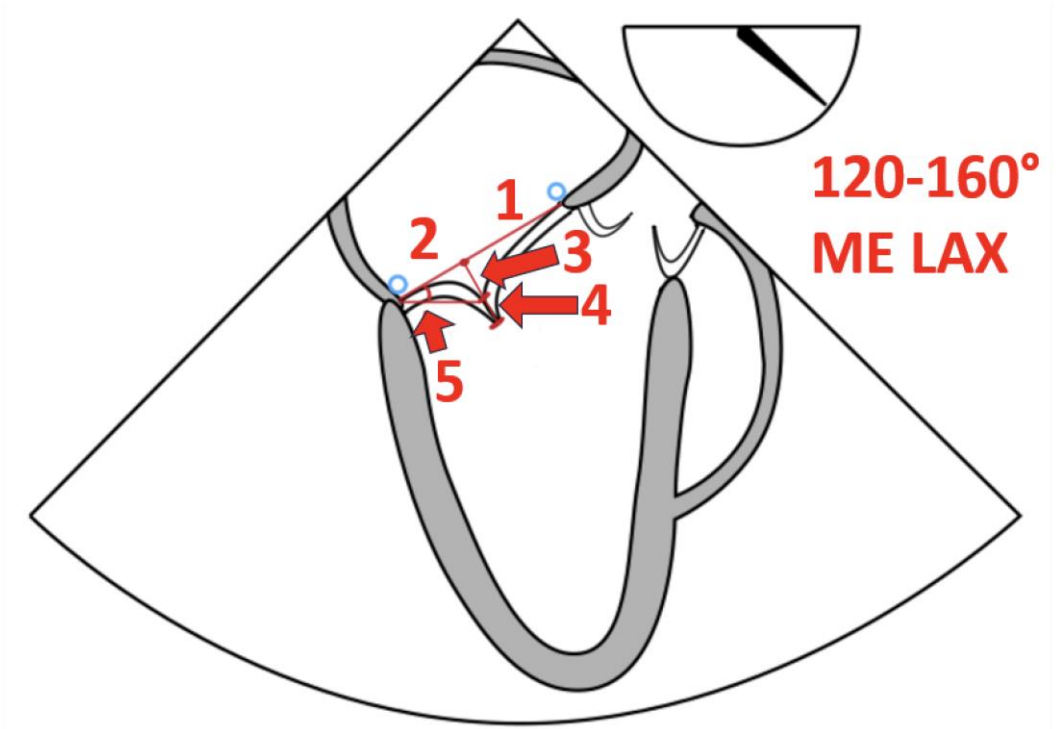
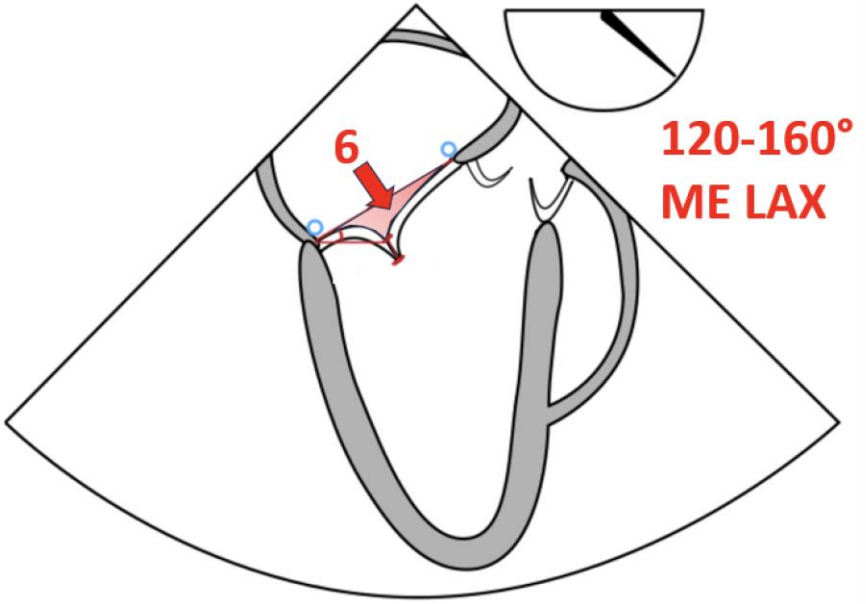
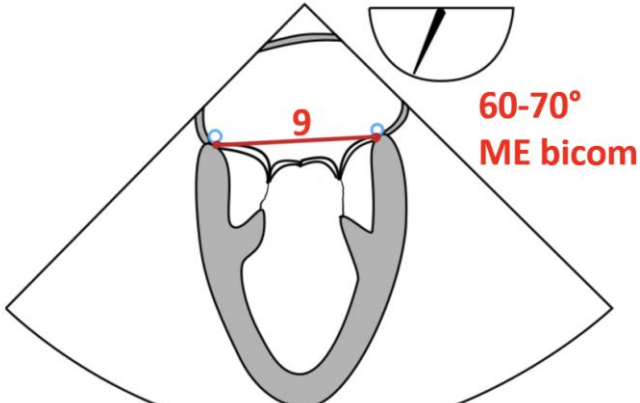
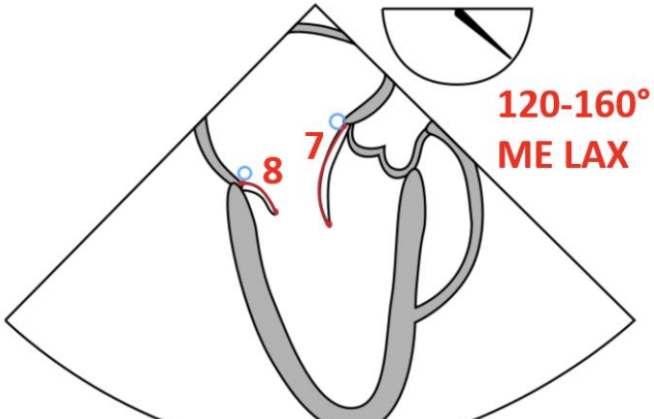
Appendix 2





Ratio 1. and 2. describes the coaptation position





1: anterior MV leaflet position in the annular plane

2: posterior MV leaflet position in the annular plane

3: coaptation depth

4: coaptation length

5: posterior MV leaflet angle

6: tenting area

7: anterior MV leaflet length (diastole)

8: posterior MV leaflet length (diastole)

9: intercommissural distance (bicommissural)