

# INPLASY

## ACCURACY OF EXERCISE STRESS ELECTROCARDIOGRAPHY AND MULTIMODALITY IMAGING FOR DETECTING CORONARY ARTERY DISEASE IN PATIENTS WITH MITRAL VALVE PROLAPSE: A SYSTEMATIC REVIEW

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Sonaglioni, A; Nicolosi, GL; Bruno, A; Lombardo, M.

### Corresponding author:

Andrea Sonaglioni

sonaglioniandrea@gmail.com

### Author Affiliation:

IRCCS MultiMedica.

### ADMINISTRATIVE INFORMATION

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**Review Stage at time of this submission** - The review has not yet started.

**Conflicts of interest** - None declared.

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**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 August 2024 and was last updated on 30 August 2024.

### INTRODUCTION

**Review question / Objective** The present systematic review has been primarily designed to summarize the main findings of the studies that evaluated the accuracy of noninvasive screening tests for detecting coronary artery disease (CAD), such as exercise electrocardiography (ECG), exercise myocardial perfusion scintigraphy (MPS) and/or exercise stress echocardiography (ESE), in individuals with mitral valve prolapse (MVP).

**Rationale** Mitral valve prolapse (MVP) has a number of clinical characteristics that can mimic coronary artery disease (CAD), such chest pain, ventricular arrhythmias (VAs) and electrocardiographic (ECG) and/or echocardiographic abnormalities, which can be recorded both at rest and during physical exercise. Even if cases of MVP and CAD are commonly encountered in the clinical practice, the prevalence

of CAD among MVP individuals has been poorly investigated. Notably, starting from 1970s, only a few number of studies have evaluated the accuracy of noninvasive screening tests for detecting CAD, such as exercise ECG, exercise myocardial perfusion scintigraphy (MPS) and/or exercise stress echocardiography (ESE), in individuals with MVP, reporting not univocal results.

**Condition being studied** Mitral valve prolapse (MVP) is the most common cardiac valvular anomaly in developed countries, affecting about 2-3% of the general population (PMID: 10387935, PMID: 12383578, PMID: 24867995). It is diagnosed as the systolic billowing of one or both mitral leaflets >2 mm above the mitral annulus into the left atrium, detected from the parasternal long-axis view during two-dimensional (2D) transthoracic echocardiography (TTE) (PMID: 10387935). Even if MVP is generally a benign condition, its clinical course may be complicated by the occurrence of complex ventricular arrhythmias

(VAs), mitral regurgitation (MR), infective endocarditis, stroke, atrial fibrillation and even sudden cardiac death (PMID: 3776983, PMID: 3335704, PMID: 31498700).

To date, most Authors have examined MVP by using resting 2D-TTE and/or exercise stress echocardiography (ESE) and/or dobutamine stress echocardiography for evaluating the mitral regurgitation (MR) degree secondary to MVP and its potential impact on pulmonary hemodynamics (PMID: 15209729, PMID: 17386112) and for a prognostic risk stratification of MVP individuals over a mid-to-long term follow-up period (PMID: 24396041, PMID: 25672368).

## METHODS

**Search strategy** A comprehensive search of all studies examining the specificity and sensitivity of exercise ECG and/or exercise MPS and/or ESE in detecting obstructive CAD in MVP patients, will be carried out by two independent reviewers through September 2024, by using Medline and EMBASE databases. The search strategy will include the following terms: “mitral valve prolapse” AND “coronary artery disease” AND “exercise electrocardiography” OR “exercise myocardial perfusion scintigraphy” OR “exercise stress echocardiography” AND “false positive result” OR “specificity” AND “false negative result” OR “sensitivity”. Search will be limited to full-text articles published in English. There will be no limitation of time period.

**Participant or population** Individuals with mitral valve prolapse who underwent exercise ECG and/or exercise MPS and/or ESE for suspected CAD.

**Intervention** Noninvasive screening tests for detecting coronary artery disease (CAD), such as exercise electrocardiography (ECG), exercise myocardial perfusion scintigraphy (MPS) and/or exercise stress echocardiography (ESE) performed in individuals with mitral valve prolapse (MVP) with suspected CAD.

**Comparator** Comparison of sensitivity and specificity of the following techniques: exercise electrocardiography (ECG), exercise myocardial perfusion scintigraphy (MPS) and/or exercise stress echocardiography (ESE), performed in MVP individuals with suspected CAD.

**Study designs to be included** Observational Cohort and Cross-Sectional Studies.

**Eligibility criteria** All studies assessing the specificity and sensitivity of exercise ECG and/or

exercise MPS and/or ESE in detecting obstructive CAD in MVP patients, will be included. Conversely, studies conducted on MVP individuals that did not analyze the accuracy of noninvasive screening tests for diagnosing obstructive CAD, studies that analyzed MVP patients by one of the above-mentioned coronary provocative tests without coronary angiography data, non-clinical articles, animal studies, duplicate articles, case reports, conference presentations, reviews, correspondences, editorials, letters without data, and abstracts, will be excluded.

**Information sources** Medline and EMBASE databases.

**Main outcome(s)** The present systematic review has been primarily designed to summarize the main findings of the studies that evaluated the accuracy of noninvasive screening tests for detecting coronary artery disease (CAD), such as exercise electrocardiography (ECG), exercise myocardial perfusion scintigraphy (MPS) and/or exercise stress echocardiography (ESE), in individuals with mitral valve prolapse (MVP).

### Quality assessment / Risk of bias analysis

Articles included in this systematic review will be assessed for risk of bias (RoB) using the National Institutes of Health (NIH) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies. All the studies will be assigned a “yes”, “no”, or “other” to each of the 14 criteria outlined in the appraisal tool. Then, by considering each criterion, the investigators will evaluate the overall quality of the study and assigned an overall “good” (met 11–14 criteria), “fair” (met 6–10 criteria), “poor” (met 0–5 criteria) rating to each study. The quality rating will be independently estimated by two authors. Disagreement will be resolved by consensus.

**Strategy of data synthesis** Two reviewers will screen the databases according to the inclusion criteria and perform data extraction independently. Following information concerning MVP individuals: 1) demographics (age and sex); 2) resting ECG data, particularly ST-T-wave abnormalities in inferolateral leads; 3) the method used for MVP diagnosis (phonocardiography, M-mode echocardiography, left ventricular cineangiography or 2D-echocardiography) and the degree of MR associated with MVP; 4) the type/s of coronary provocative test/s used in each study (exercise ECG and/or exercise MPS and/or ESE); 5) data concerning exercise-induced symptoms (particularly chest pain) and/or ventricular premature beats (VPBs); 6) finally, the estimated

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specificity and sensitivity of each coronary provocative test for all the included studies; will be independently collected by the two reviewers. A third author (G.L.N.) will check the extracted data for accuracy and resolve possible discrepancies between reviewers.

**Subgroup analysis** The accuracy of noninvasive screening tests for detecting coronary artery disease (CAD), such as exercise electrocardiography (ECG), exercise myocardial perfusion scintigraphy (MPS) and/or exercise stress echocardiography (ESE), in individuals with mitral valve prolapse (MVP) will be separately analyzed.

**Sensitivity analysis** N/A.

**Country(ies) involved** Italy.

**Keywords** Mitral valve prolapse; coronary artery disease; coronary provocative tests; sensitivity; specificity.

#### **Contributions of each author**

Author 1 - Andrea Sonaglioni - Design of the manuscript, acquisition, analysis and interpretation of the data, drafting of the manuscript.

Email: sonaglioniandrea@gmail.com

Author 2 - Gian Luigi Nicolosi - Design of the manuscript, acquisition, analysis and interpretation of the data, drafting of the manuscript.

Email: gianluiginicolosi@gmail.com

Author 3 - Antonino Bruno - Design of the manuscript, acquisition, analysis and interpretation of the data, drafting of the manuscript.

Email: antonino.bruno@multimedica.it

Author 4 - Michele Lombardo - Supervision.

Email: michele.lombardo@multimedica.it