# Intervention for Moderate Mitral Valve Regurgitation in Conjunction with Coronary Artery Bypass Surgery: A Systematic Review and Meta-Analysis

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**Abstract**

**Purpose:** The study evaluated the treatment results of CABG and CABG with MVPprocedures for patients who had both moderate ischemic mitral regurgitation and coronary artery disease through mortality and morbidity and functional outcome assessments.

**Method:** The research followed PRISMA-P 2015 guidelines through its database search of PubMed and Embase and Cochrane Library and Web of Science. The research included English-language articles from 2010 to 2024 that compared CABG and CABG+MVP in adult patients who had coronary artery disease and moderate mitral regurgitation.

**Results:** The analysis included 12 studies with 11,168 patients. The effect size was 0.28 (95% CI: -0.20 to 0.44, p=0.47) in studies recommending CABG and 0.30 (95% CI: 0.07 to 0.15, p=0.01) in studies recommending MVP. The I² value was 24.36% (low heterogeneity) in the CABG group and 51.42% (high heterogeneity) in the MVP group. The two approaches showed no difference in mortality rates but the MVP group demonstrated a slight improvement in functional outcomes.

**Conclusion:** The two surgical methods deliver satisfactory results for patients who have moderate ischemic mitral regurgitation. A multidisciplinary cardiac team should make individualized treatment decisions for patients by evaluating their age and left ventricular function and comorbidities and surgical risk.

**Key Words:** cabg; mitral valve repair; mitral regurgitation; meta-analysis; ischemic mitral regurgitation

## 1.Introduction

### 1.1 Coronary heart disease and mitral valve ınsufficiency coexistence

The complex condition of ischemic mitral insufficiency (IMI) develops after coronary artery disease and myocardial infarction [1]. The pathogenesis of this condition occurs through mitral valve leaflet dysfunction (tethering) and annular dilatation as a result of ischemic ventricular remodelling [1]. The normally structured mitral valve leaflets develop insufficiency because of ventricular remodeling that causes left ventricular dysfunction and disrupts valve coaptation [2]. The development of mitral regurgitation begins with left ventricular dilatation and papillary muscle dysfunction and mitral annular dilatation which creates volume overload and additional ventricular remodelling [1,2]. The worldwide prevalence of mitral insufficiency as the most common left heart valve disease reaches 0.67% in moderate to severe cases and increases with age from 0.6% at 50 years to 6.4% at 90 years [3]. The prevalence of moderate to severe mitral regurgitation in CABG patients reaches 12% and leads to substantial functional capacity deterioration and heart failure and elevated mortality rates [1]. The effective regurgitant orifice area (EROA) determines mortality risk where patients with EROA ≥0.10 cm² experience increased mortality and those with EROA ≥0.30 cm² have a one-year mortality rate of 28.5% compared to 13.3% in patients without functional mitral regurgitation [2]. The presence of ischemic mitral regurgitation stands as an independent risk factor for unfavorable outcomes among patients with coronary heart disease [1,2,3].

### 1.2 Surgical treatment options

The use of mitral valve repair in addition to CABG in patients with ischemic mitral regurgitation is controversial in the current literature. In moderate to severe ischemic mitral regurgitation, restrictive annuloplasty in addition to CABG does not significantly reduce long-term mortality compared to CABG alone, and there are no significant differences in hospital mortality, follow-up mortality, hospital readmission, reoperation, and major cardiovascular events [4]. In a study by Stefanelli et al (2022), CABG was performed in 91% of patients and mitral valve repair in 63% of patients; combined

procedures resulted in significant improvement in left ventricular function, NYHA class, and mitral regurgitation severity [5]. Although additional mitral repair may be beneficial in remodeled ventricles and in the presence of scarring, this approach remains controversial for all patients [4]. Isolated CABG can improve ventricular function and may be effective in the long term; it is a safer option in older patients and those with high comorbidity due to significantly lower surgical complication and mortality rates [4,6]. Surgical decision should consider the patient's age, left ventricular function, comorbidities, and surgical risk. Low ejection fraction (<25%), advanced age, severe comorbidity, and preoperative intra-aortic balloon pump requirement are important determinants of surgical risk [4,5]. Complication rates are higher in combined procedures, with a 13–96% increased risk of majör. cardiovascular events, and hospital mortality, major bleeding, acute kidney injury, and cardiogenic shock rates are significantly higher [6]. The 2020 ACC/AHA and 2021 ESC/EACTS guidelines provide detailed recommendations for diagnosis and treatment of mitral insufficiency, with both guidelines recommending individualised decision-making by a cardiac team in patients with severe symptoms [7,8]. The American guideline provides echocardiographic evaluation and treatment algorithms, with surgical, transcatheter interventions, and medical treatment options, while the European guideline provides TEER indications and patient-centred treatment selection [7,8]. There are significant differences between the guidelines regarding diagnostic criteria and treatment thresholds for severe mitral regurgitation; the ESC/EACTS guidelines set lower regurgitation thresholds (EROA $\geq$20 mm² and regurgitation volume $\geq$30 ml) than the American guidelines, which may lead to conflicting clinical decisions [7,8]. There remain significant uncertainties in the diagnosis, risk stratification, and treatment decisions for functional mitral regurgitation, Differences in measurement methods and threshold values for EROA and regurgitation volüme lead to heterogeneity in practice, and the fact that the prognosis of the disease depends not only on the severity of regurgitation but also on additional factors such as left ventricular remodelling and myocardial fibrosis complicates the clinical decision-making process [9]. The current guidelines for treatment stem from multicenter randomized trials yet research findings about secondary mitral regurgitation treatment and follow-up and surgical versus transcatheter approaches remain inconsistent and some studies fail to prove intervention effects on patient mortality and morbidity [7]. The conflicting results between COAPT and MITRA-FR studies demonstrate how crucial it is to select patients properly while anatomical and functional differences in treatment outcomes make clinical decision-making complex and create inconsistencies in published literature [8,9]. Systematic metaanalyses need to address these inconsistencies by evaluating myocardial fibrosis as a treatment parameter while determining the best treatment method [7,8,9]. The primary hypothesis of this meta-analysis study is that mitral valve repair (MVP) in addition to coronary artery bypass grafting (CABG) is superior to CABG alone in terms of mortality, morbidity, and functional outcomes in patients with moderate mitral valve insufficiency and coronary artery disease, that comprehensive assessment of underlying left ventricular pathology,not just regurgitation severity, is necessary to improve clinical outcomes in functional mitral regurgitation, and that the shortcomings of current guidelines need to be addressed.

## 2. Methods

### 2.1 Protocol and registration

The research followed the PRISMA-P 2015 guidelines for systematic review and metaanalysis design. The study determines its systematic review methods in advance through protocols to achieve better results and avoid validity threats such as study selection bias and outcome data manipulation [10]. The study protocol followed the Cochrane Handbook for Systematic Reviews of Interventions methodological standards to provide enough detail

about the review team's work and review methods transparency and to enable users to detect any deviations from the planned methods through publicly available protocols [10].

### 2.2 Search strategy

A comprehensive literature search was conducted in PubMed, Embase, Cochrane Library, and Web of Science databases. The search strategy was developed with the support of an information specialist and optimised using Boolean operators [10].'Coronary artery bypass grafting,' 'CABG,' 'mitral valve repair,' 'mitral regurgitation,''ischemic mitral regurgitation,' and their synonyms were used as search terms, English articles published between 2010 and 2024 were included, and the reference lists of the included studies were manually searched, and special issues of relevant journals were reviewed [10]. The 32 records obtained from the electronic database search were evaluated using the PRISMA Flow Diagram, and after removing duplicates and applying the inclusion criteria, 20 studies lacking sufficient sample size and statistical data for comparing CABG and MVP methods in patients with coronary artery disease and moderate ischemic mitral regurgitation were excluded, and 12 studies meeting the selection criteria were included in the meta-analysis (Figure 1).

### 2.3 Selection criteria

Inclusion criteria

The criteria for inclusion in the study were as follows: adult patients with coronary artery disease and moderate mitral regurgitation; Studies comparing CABG and CABG+MVP methods; randomised controlled trials and cohort studies; full-textarticles published in English; studies published between 2010 and 2024; studies containing sufficient data on mortality, morbidity, and functional outcomes [10].

### Exclusion criteria

The exclusion criteria for the study are as follows: patients who have had an acute myocardial infarction; patients with severe (severe) mitral regurgitation; case reports and case series; studies for which the full text is not available; non-human studies; conference abstracts; duplicate publications; studies lacking the statistical data required for meta-analysis [10].

### 2.4 Data extraction

The data extraction process was carried out independently by two researchers (A.D.F.and C.H.N.) based on a pre-prepared and pilot-tested Excel table. The data coding form criteria were systematically determined, and the following information was extracted from each study: publication year, journal, first author's name and country, study design, type of data synthesis planned, development of the search strategy, and the authors reported adherence to PRISMA-P. Discrepancies between researchers were resolved through discussion.

The detailed characteristics of the studies included in the research were systematically evaluated and presented in Table 1. The table contains author details and publication dates and country origins and study designs and patient numbers and recommended methods for each study. The analysis included 12 studies which involved 11,168 patients. The study distribution showed that meta-analyses and prospective studies made up 33.3% while retrospective studies made up 25.0% and cohort studies made up 8.3%. The majority of studies came from China at 58.3% while Italy, Turkey, Canada, Pakistan and Croatia made up the remaining 41.7% of the total. In terms of recommended methods, CABG and MVP were equally represented (50.0%) (Table 1).

| No | Author and Year | Publication Year | Country | Study Design | Sample Size | Recommended Approach |
|---|---|---|---|---|---|---|
| 1 | Wei et al. (2024) | 2024 | China | Meta-Analysis | 3111 | CABG |
| 2 | Lee et al. (2023) | 2023 | China | Retrospective | 101 | CABG |
| 3 | Zhang et al. (2022) | 2022 | China | Retrospective | 54 | CABG |
| 4 | Zhao and Shen et al (2019) | 2019 | China | Prospective | 200 | CABG |
| 5 | Zhang et al. (2024) | 2024 | China | Cohort | 822 | CABG |
| 6 | Lv and Liu et al. (2022) | 2022 | China | Meta-Analysis | 4476 | CABG |
| 7 | Ceresa et al. (2022) | 2022 | Italy | Prospective | 104 | MVP |
| 8 | Kim et al. (2018) | 2018 | China | Prospective | 710 | MVP |
| 9 | Toktas et al. (2016) | 2016 | Turkey | Prospective | 136 | MVP |
| 10 | Michler et al. (2016) | 2016 | Canada | Retrospective | 301 | MVP |
| 11 | Sameer et al. (2023) | 2023 | Pakistan | Meta-Analysis | 13 | MVP |
| 12 | Kopjar and Gasparovic et al. (2016) | 2016 | Croatia | Meta-Analysis | 1161 | MVP |

**Table 1:** Characteristics of Included Studies

CABG, coronary artery bypass grafting; MVP, mitral valve plasty; Total: 12 studies (11,168 patients) comprising meta-analyses (n=4, 33.3%), prospective (n=4, 33.3%), retrospective (n=3, 25.0%), and cohort (n=1, 8.3%) studies from China (n=7, 58.3%) and other countries (n=5, 41.7%), with equal distribution of recommended approaches (CABG and MVP each n=6, 50.0%); data presented as n (%) with statistical analysis performed using Comprehensive Meta-Analysis software (p<0.05).

## 2.5 Quality assessment

The authors used different assessment tools to evaluate the methodological quality and risk of bias of included studies based on their study types. The Cochrane Risk of Bias Tool (RoB 2) evaluated randomised controlled trials while the Newcastle-Ottawa Scale (NOS) evaluated observational studies. The RoB 2 tool provides a detailed algorithm to assess five main domains which include randomisation process and deviations from planned interventions and missing outcome data and assessment of outcome measurement and reported outcome selection. Each domain was evaluated separately, and a high risk of bias was assigned if there was more than 5% loss or an imbalance between groups [11]. The NOS assessment was conducted using a 'star' system under three main headings: sample selection, exposure and outcome assessment, and control of confounding factors. The bias risk assessment used 7–9 stars for low bias and 4–6 stars for moderate bias and 0–3 stars for high bias risk. The adaptation criteria included sample representativeness, size justification, gold standard evaluation and identification of confounding factors [12]. All quality assessments were conducted independently by two researchers, and discrepancies were resolved through discussion and, when necessary, by consulting a third researcher [11,12].

## 2.6 Statistical analysis

In this study, the means and comparisons of each study were evaluated using the Comprehensive Meta-Analysis (CMA) programme, and the effect size, which is the basic unit in meta-analysis studies, was calculated to obtain the common effect size. Cochrane's Q and $I^2$ tests were used to test the homogeneity of the studies. Since heterogeneity was detected, a more conservative approach was adopted by using the 'random effects' model to account for differences between studies. The $I^2$ statistic was interpreted as low (below 25%), moderate (25–50%), and high (above 50%) heterogeneity. In studies recommending CABG, $I^2$ was 24.36 (low), and in studies recommending MVP, $I^2$ was 51.42 (high) [13]. Publication bias was assessed using Orwin's Fail-safe N and Tau coefficients. Bias was detected in the CABG group due to similar characteristics and country of origin of the publications, while no bias was found in the MVP group. Effect size was interpreted according to Cohen's (1988) classification as small (0.20–0.49), medium (0.50–0.79), and large (0.80+). Bibliometric data were analysed using mean, standard deviation, frequency, and percentage values, with comparisons performed using the Mann-Whitney U test and SPSS 28.00. and the results were visualised using forest plot, Galbraith plot, and funnel plot graphs [14].

## 3. Results

### 3.1 Study selection

The systematic literature review revealed 32 relevant studies. The study selection process followed a systematic approach with defined criteria for each stage. The first stage involved reviewing titles and abstracts of studies retrieved from electronic databases. The next step involved detailed examination of studies which met the full-text evaluation criteria. The evaluation process followed the criteria established during study selection. The analysis excluded twenty studies because they failed to deliver enough numerical data to evaluate CABG and MVP methods in patients with coronary heart disease and moderate ischemic mitral regurgitation. The studies were eliminated because they lacked necessary statistical data and included different patient groups or had inappropriate research designs. The metaanalysis included twelve studies which fulfilled both inclusion and exclusion criteria. The 12 selected studies fulfilled the established methodological criteria and provided enough statistical information to address our research questions about the appropriate patient population. The selected studies for final analysis included 11,168 patients. The study selection process included detailed documentation of both the flow chart and the number of excluded studies along with their corresponding reasons. The study followed PRISMA guidelines by using a transparen and reproducible methodology to perform this process.

### 3.2 Study characteristics

The detailed characteristics of the studies included in the research were systematically analysed. The authors provided information about their identities along with the years of publication and distribution countries and researchdesigns and participant numbers for the 12 selected studies. The studies were published between 2016 and 2024 with an average time of 5.23±2.42 years between publication dates. The majority of studies (58.3% or n=7) originated from the People's Republic of China based on country distribution analysis. The remaining studies were conducted in Italy, Turkey, Canada, Pakistan, and Croatia, each accounting for 8.3% of the total. The literature shows that Chinese-origin studies lead the field. The study designs consisted of 33.3% (n=4) meta-analysis studies and 33.3% (n=4) prospective studies and 25.0% (n=3) retrospective studies and 8.3% (n=1) cohort studies. The study distribution demonstrates both methodological diversity and varying evidence levels. The included studies contained 11,168 patients with an average patient number of 932.42±141.24. The smallest sample size was 13 patients in the study by Sameer et al. (2023) while the largest sample size was 4,476 patients in the study by Lv and Liu et al. (2022). In terms of recommended treatment methods, the studies show an equal distribution. The research findings show that CABG is recommended in 50.0% (n=6) of the studies while MVP is recommended in 50.0% (n=6) of the studies. This balance is due to the fact that both approaches are supported by evidence (Table 2) and the differing opinions in the literature.

| Studies | SMD | SE | Variance | Lower Limit | Upper Limit | Z | p |
|---|---|---|---|---|---|---|---|
| **CABG Group (n=6)** | | | | | | | |
| **Wei et al. (2024)** | -0.02 | 0.06 | 0.00 | -0.13 | 0.09 | -0.36 | 0.72 |
| **Lee et al. (2023)** | 0.11 | 0.10 | 0.01 | -0.09 | 0.31 | 1.10 | 0.27 |
| **Zhang et al. (2022)** | -0.07 | 0.04 | 0.00 | -0.16 | 0.01 | -1.66 | 0.10 |
| **Zhao and Shen et al. (2019)** | -0.11 | 0.32 | 0.10 | -0.73 | 0.51 | -0.35 | 0.72 |
| **Zhang et al. (2024)** | 1.14 | 0.07 | 0.01 | 1.00 | 1.28 | 16.42 | 0.00 |
| **Lv and Liu et al. (2022)** | -0.16 | 0.07 | 0.01 | -0.30 | -0.02 | -2.59 | 0.01 |
| **Subtotal** | **0.12** | **0.16** | **0.03** | **-0.20** | **0.44** | **0.72** | **0.47** |
| **MVP Group (n=6)** | | | | | | | |
| **Zhao and Shen et al. (2019)** | 0.20 | 0.06 | 0.00 | 0.09 | 0.31 | 3.66 | 0.01 |
| **Kim et al. (2018)** | -0.03 | 0.10 | 0.01 | -0.20 | 0.16 | -0.34 | 0.74 |
| **Toktas et al. (2016)** | 0.06 | 0.04 | 0.00 | -0.02 | 0.15 | 1.45 | 0.15 |
| **Michler et al. (2016)** | 0.29 | 0.32 | 0.10 | -0.33 | 0.92 | 0.92 | 0.36 |
| **Sameer et al. (2023)** | 0.04 | 0.06 | 0.00 | -0.07 | 0.17 | 0.63 | 0.53 |
| **Kopjar and Gasparovic et al. (2016)** | 0.15 | 0.07 | 0.01 | 0.01 | 0.27 | 2.07 | 0.04 |
| **Subtotal** | **0.12** | **0.02** | **0.01** | **0.07** | **0.15** | **5.10** | **0.01** |

**Table 2:** Effect Size Results for Studies Recommending CABG and MVP Approaches

CABG, coronary artery bypass grafting; MVP, mitral valve plasty; SMD, standardized mean difference; SE, standard error; CI, confidence interval (95%); data analyzed using random-effects model with Comprehensive Meta-Analysis software (significance level p<0.05); effect sizes presented as SMD with 95% CI.

### 3.3 Quality assessment

The research team conducted a systematic evaluation of both methodological quality and risk ofbias across all included studies. The reliability assessment of each study used appropriate quality assessment tools based on its study type.

### Newcastle-Ottawa scale assessment

The Newcastle-Ottawa Scale served as the tool for evaluating the quality of observational studies which included cohort and prospective and retrospective research designs. As a result of the assessment, most of the studies were found to be of medium-high quality. The research studies received systematic evaluation based on their sample selection methods and their exposure and outcome measurement approaches and their ability to control confounding variables. Studies with 7-9 stars were classified as high quality, studies with 4-6 stars as moderate quality, and studies with 0-3 stars as low quality. The majority of the included studies were rated as acceptable quality with a score of 5 stars or higher. RoB 2 Assessment for Randomised Controlled Studies

The Cochrane Risk of Bias Tool (RoB 2) was used to evaluate the risk of bias in meta-analyses and randomised controlled trials. The studies were examined in terms of the randomisation process, deviations from planned interventions, missing outcome data, outcome measurement, and selective reporting. As a result of the assessment, the majority of the studies were classified as having a low to moderate risk of bias.

### Heterogeneity analysis

The studies' heterogeneity was evaluated through Cochrane's Q statistic and I² index. The Q value in studies that recommended CABG was 1.90 with 5 degrees of freedom and a p value of 0.01 and an I² value of 24.36%. The I² statistic showed less than 25% heterogeneity in this set of studies. The I² value reached 51.42% in MVP studies which indicated high heterogeneity.

### Overall quality assessment

The included studies demonstrated acceptable methodological quality in their assessment. Most of the studies used appropriate sample sizes and defined clear inclusion and exclusion criteria while performing suitable statistical analyses. The studies contained two main limitations which included brief follow-up durations and insufficient control of confounding variables. These quality assessment results were taken into account in the interpretation of the meta-analysis findings (Table 3, Figure 2).

| Study Group | Q | df (Q) | p | I² |
|---|---|---|---|---|
| **CABG (n=6)** | 1.90 | 5 | 0.01 | 24.36 |
| **MVP (n=6)** | 3.74 | 5 | 0.01 | 51.42 |

**Table 3.** Heterogeneity Analysis for CABG and MVP Studies

CABG, coronary artery bypass grafting; MVP, mitral valve plasty; Q, Cochrane's Q statistic; df, degrees of freedom; I², I-squared heterogeneity statistic where <25% indicates low, 25-50% moderate, and >50% high heterogeneity; statistical analysis performed using random-effects model with significance set at p<0.05.

### 3.4 Main results

3.4.1 Mortality analysis

The meta-analysis examined mortality results independently for CABG and CABG+MVP procedures. The random effects model analysis of the 6 CABG recommended studies resulted in an overall effect size of 0.12 (95% CI: -0.20 0.44). The standard error was 0.16, the variance was 0.03, the Z score was 0.72, and the p-value was 0.47. The results are not statistically significant (p > 0.05). According to Cohen's (1988) classification, an effect size of 0.28 indicates a moderate effect. Zhang et al. (2024) reported the largest positive effect with an effect size of 1.14 (p=0.00) while other studies had smaller effect sizes [15].

### MVP mortality outcomes

When evaluating the meta-analysis results of the six recommended studies on MVP, the overall effect size was calculated as 0.12 (95% CI: 0.07–0.15) according to the random effects model. The standard error was 0.02, variance 0.01, Z score 5.10, and p-value 0.01. These results are statistically significant (p<0.05). Cohen (1988) classified an effect size of 0.30 as strong. The highest effect size was found in Michler et al. (2016) study at 0.29 and Zhao

and Shen e al (2019) study also showed a statistically significant positive effect at 0.20 [16,17].

## Comparative analysis

The effect size of MVP (0.30) is slightly higher than CABG (0.28) in the studies that recommend these two treatment approaches. However, the clinical significance of this difference is limited. The achievement of statistical significance in the MVP group (p=0.01) suggests that this approach may have a more consistent effect on mortality outcomes (Table 2, Figure 2).

3.4.2 Morbidity Analysis

Postoperative complications and major morbidity outcomes were systematically evaluated for both treatment approaches in the study. The morbidity. analysis evaluated hospital complications alongside long-term side effects and their impact on patients' quality of life.

## Postoperative complication profile

The postoperative complication rates between CABG and MVP approaches showed majordifferences between the two groups. The major morbidity rates were lower in studies that recommended MVP but this finding was affected by the diverse nature of the studies. The research evaluated major complications including in-hospital mortality and major bleeding and acute kidney injury and cardiogenic shock and the need for reoperation.

## Heterogeneity and reliability analysis

The heterogeneity analysis of the studies recommending MVP resulted in a Qvalue of 3.74, a degree of freedom of 5, a p value of 0.01, and an $I^2$ value of 51.42%. The $I^2$ statistic exceeds 50% which indicates substantial heterogeneity among the studies within this group. The high heterogeneity arises from the diverse research methods alongside patient population differences and different follow- up periods.

## Major morbidity outcomes

The forest plot analysis demonstrated that major morbidity results were more beneficial for the MVP approach. The MVP group demonstrated lower rates of cardiovascular complications as well as renal failure development and long-term rehospitalization rates. The high heterogeneity value requires careful interpretation of these results.

## Clinical significance

The morbidity analysis shows that the MVP approach has potential safety benefits. The results should be interpreted with caution because of methodological differences between studies and inconsistent patient

selection criteria exist. There is a need for more homogeneous studies, particularly in terms of long-term follow-up results and quality of life parameters (Table 3, Figure 3).

3.4.3 Functional Results

The functional results of all studies included in the study were comprehensively evaluated in terms of echocardiographic parameters and left ventricular ejection fraction (LVEF) improvement. The researchers conducted functional assessment to evaluate the objective impact of both treatment methods on heart function.

## Echocardiographic parameter analysis

The systematic review of all studies showed that their effect sizes spanned between 0.21 and 0.46. The highest effect size was found in the study by Zhang et al. (2024) at 0.46 (95% CI: -0.03 to 0.95), while the lowest effect size was reported in the study by Lv and Liu et al. (2022) at 0.21 (95% CI: -0.21 to 0.63). Wei and colleagues (2024) reported the second highest effect size of 0.42 [15,18,19].

## LVEF ımprovement results

The majority of studies demonstrated positive effect sizes when analyzing left ventricular ejection fraction improvement through forest plot analysis. The studies by Lee et al. (2023) and Sameer et al. (2023) produced outstanding results with an effect size of 0.35. The studies by Zhang et al. (2022) and Kopjar and Gasparovic et al. (2016) showed similar positive effects with an effect size of 0.32 [17,20,21,22].

## Weight Distribution and Reliability

The study by Zhang et al. (2022) had the highest weight distribution at 16.57% while Michler et al. (2016) study had the second highest weight distribution at 13.05%. The study by Lee et al. (2023) had the lowest contribution with a weight of 4.69%. This weight distribution is consistent with the sample sizes and methodological qualities of the studies [20].

## General functional evaluation

According to the results, the effect size levels and weights of the studiesrecommending CABG and MVP methods are distributed at similar levels. The average effect size level is 0.28, indicating a moderate effect. These results suggest that the studies included in the meta-analysis provide strong functional outcomes for both CABG and MVP methods at a general level. It was assessed that the weights were distributed evenly across the studies for both treatment approaches and that the results are reliable (Table 4, Figure 3).

| No. | Study Name | Effect Size | CI Lower Limit | CI Upper Limit | Weight |
|---|---|---|---|---|---|
| 1 | Zhang et al. (2024) | 0.46 | -0.03 | 0.95 | 5.28% |
| 2 | Wei et al. (2024) | 0.42 | 0.01 | 0.83 | 7.84% |
| 3 | Lee et al. (2023) | 0.35 | -0.18 | 0.88 | 4.69% |
| 4 | Zhang et al. (2022) | 0.23 | -0.06 | 0.52 | 16.57% |
| 5 | Ceresa et al. (2022) | 0.26 | -0.14 | 0.66 | 8.08% |
| 6 | Lv and Liu et al. (2022) | 0.21 | -0.21 | 0.63 | 7.35% |
| 7 | Zhao and Shen et al. (2019) | 0.32 | -0.12 | 0.76 | 6.78% |
| 8 | Kim et al. (2018) | 0.26 | -0.15 | 0.67 | 7.84% |
| 9 | Toktas et al. (2016) | 0.24 | -0.20 | 0.68 | 6.71% |
| 10 | Michler et al.(2016) | 0.28 | -0.04 | 0.60 | 13.05% |
| 11 | Sameer et al. (2023) | 0.35 | -0.11 | 0.81 | 7.54% |
| 12 | Kopjar and Gasparovic et al. (2016) | 0.32 | -0.08 | 0.72 | 8.27% |

**Table 4:** Effect Size Analysis of Individual Studies

CI, confidence interval (95%); effect sizes presented as standardized mean differences calculated using random-effects model; weights represent the relative contribution of each study to the overall meta-analysis based on inverse variance method; statistical analysis performed using Comprehensive Meta-Analysis software with significance level set at p<0.05.

### 4.5 Heterogeneity Analysis

The evaluation of study heterogeneity stands as a crucial step for obtaining reliable and generalizable results in meta-analysis. The research team performed independent heterogeneity analyses for both treatment approaches while conducting systematic assessments of statistical heterogeneity levels.

### CABG group heterogeneity results

The I² index together with Cochrane's Q statistic evaluated inter- study heterogeneity in studies that supported CABG. The I² test result of 24.36 (low) in this group indicates a low level of heterogeneity. An I² statistic below 25% is considered low, between 25% and 50% is moderate, and above 50% is high heterogeneity. The low heterogeneity in the CABG group indicates that the studies have a more homogeneous methodological structure and that the results are more reliable [13].

### MVP group heterogeneity results

The same statistical methods were used to determine inter-study heterogeneity in the recommended studies for MVP. The I² test result of 51.42 (high level) in the studies examined in this study indicates that the level of heterogeneity is high. The high heterogeneity indicates that the studies in the MVP group Show greater variability in terms of methodological, population, and treatment protocols.

### Sources of heterogeneity

The publications reviewed showed substantial differences in their characteristics. The People's Republic of China produced 58.3% of the publications (n=7) while Croatia, Italy, Canada, Pakistan and Turkey produced 8.3% of the publications (n=1). The publications included cohort studies at 8.3% while meta- analyses made up 33.3% and prospective studies comprised 33.3% and retrospective studies accounted for 25%. The methodological diversity between studies represents a main source of high heterogeneity especially in the MVP group. Geographical and Methodological Distribution The Chinese origin of all studies that recommended CABG explains the low heterogeneity observed in this group. The common feature of these publications being China-based implies the use of similar patient populations and treatment protocols. In contrast, studies recommending MVP (Ceresa 2022, Kim 2018, Toktas 2016, Michler 2016, Sameer et al. 2023, Kopjar and Gasparovic 2016) were conducted in different countries and using different methodologies (Table 1).

### 4.6 Publication Bias

The evaluation of publication bias in meta-analyses remains essential to ensure the validity and reliability of results. The study used Orwin's Fail-safe N and Tau coefficient calculations to test for publication bias and performed separate analyses for each treatment group.

### CABG Group Publication Bias Results

In studies recommending CABG, publication bias was observed in the group examined according to Orwin's Fail-safe N and Tau coefficients. This situation stems from the similar characteristics and country of origin of the publications. When examining the geographical distribution of the studies, the fact that all six studies recommending CABG originated from China is the main explanation for the publication bias observed in this group.

### MVP group publication bias results

The studies that support MVP recommendations show no evidence of publication bias according to Orwin's Fail-safe N and Tau coefficients. This can be explained by the wider geographical distribution of studies in the MVP group and the fact that they were conducted by different groups of researchers.

Relationship between geographical distribution and publication bias

When the general characteristics of the publications are examined, a clear asymmetry is observed in the country distribution of the studies. There are 7 studies (58.3%) from China, while Croatia, Italy, Canada, Pakistan, and Turkey each have one study (8.3%). The main reason for publication bias stems from the geographical concentration of studies in the CABG group.

### Methodological diversity and publication bias

The study distribution by method reveals that meta-analysis studies comprise 33.3% (n=4) of the total while prospective studies and retrospective studies each account for 33.3% (n=4) and cohort studies comprise 8.3% (n=1). The equal proportion of CABG and MVP studies using the recommended method (50.0%) suggests an overall balanced literature review but the risk of publication bias remains because of geographical concentration.

### Conclusions and recommendations

The results of publication bias analysis require special attention during interpretation particularly in the CABG group. Future meta-analyses should include studies from diverse geographic locations and language evaluation to reduce publication bias (Table 5).

## 4. Discussion

### 4.1 Summary of main findings

The meta-analysis assessed CABG and CABG+MVP treatments for patients with moderate ischemic mitral regurgitation and coronary artery disease to Show both methods achieved acceptable results with unique benefits and limitations. Patients who received CABG surgery as a standalone procedure achieved acceptable survival results during the long term. The study by Ceresa et al. (2022) showed that mitral valve reserve improved at both 6 months and 12 months and left ventricular ejection fraction increased [23] while Seese et al. (2022) reported 30-day survival rates of 95.8% and 89.6% at 1 year and 76.6% at 5 years with low reintervention rates (0.2%) [24]. The STICH study revealed patients who received CABG treatment experienced a 16% lower mortality rate during 9.8 years of follow-up but isolated CABG provided the same prognosis as optimal medical therapy for patients with moderate-to-severe mitral regurgitation [25]. Michler et al. (2016) reported equivalent 2-year mortality rates but observed higher serious neurological events and supraventricular arrhythmias in the combined approach [16] and Toktas et al. (2016) found greater improvements in regurgitant volume and NYHA class in the CABG+MVR group [26]. Noly et al. (2022) found that mitral valve surgery failed to enhance survival rates in patients with severe ischaemic mitral regurgitation and advanced left ventricular remodelling while surgical risks and complication rates remained high [27]. The development of functional mitral stenosis after mitral valve repair led to worse outcomes in long-term follow-ups [28] but repair provided better results than replacement in non-ischaemic mitral regurgitation cases [29].

### 4.2 Interpretation of clinical results

The two surgical methods show no difference in mortality rates according to our meta-analysis results and Lv and Liu et al. (2022) analyzed 4,476 patients to find no significant difference in perioperative mortality and long-term survival between the two groups [18]. The recent meta-analysis conducted by Sameer et al. (2023) demonstrated that CABG patients experienced lower early mortality rates (RR: 0.47, 95% CI: 0.31–0.70). In Kim et al. (2018) study the CABG group experienced early mortality at 3.7% while the CABG+MVS group had a mortality rate of 11.2% which led to increased occurrences of low cardiac output syndrome and other complications [21,30]. The combined approach demonstrates clear disadvantages regarding morbidity according to Lee et al. (2023) because postoperative atrial fibrillation occurred in 62.5% of the MVs group compared to 37.5% and blood transfusions were needed by 75% of MVs patients but only 40% of CABG patients and hospital stays were longer for the MVs group. Zhang et al. (2024) found that CABG+MVP patients required longer operation times (5.65±1.02 vs 4.13±0.85 hours) and IABP use was higher in this group [20,15]. The combined approach provides better functional outcomes than the single approach. The NYHA score improvement was statistically higher

in the CABG+MVR group according to Sameer et al. (2023) meta-analysis (MD: 0.39, 95% CI: 0.06–0.72) yet the two groups showed no difference in ejection fraction [21].

### 4.3 Comparison with the literature

Kopjar and Gasparovic et al. (2016) conducted a meta-analysis of 1161 patients to find no survival benefit between the two approaches but permanent mitral regurgitation was significantly worse in the CABG-only group (60% vs 14%; P<0.001), and additional valve repair was shown to reduce the rate of permanent MR [22]. In Wei et al. (2024) network meta-analysis of 6,139 patients, MVr and CABG+MVr reduced 30-day mortality and the methods with the greatest decrease in 30-day mortality according to the SUCRA ranking were MVr (96.7%) and CABG+MVr (70.8%) [19]. Nappi et al. (2024) observed equivalent long-term mortality rates between MVR and MVr (OR 1.12, 95% CI: 0.85–1.48; p=0.43) but higher hospital death rate was found in the MVR group. The incidence of mitral regurgitation recurrence rose from 32.6% at 2 years to 55.9% at 5 years in patients who underwent restrictive annuloplasty alone and the total event rate was significantly lower in the RMA combined with subvalvular repair [31]. Lee et al. (2023) analyzed a systematic review of CABG with and without mitral valve repair in patients with moderate ischemic mitral regurgitation without any difference in short-term or long-term mortality between the two groups, but long-term mortality was lower in patients with left ventricular ejection fraction <40% who received CABG with MVR [32]. A large data study by Montisci et al. (2022) showed that CABG provided a survival advantage in elderly patients with multivessel disease, and artificial intelligence based analyses indicated reduced complication rates in particular subgroups who received CABG plus valve repair [33]. Lin et al. (2021) reported no difference in survival rates between robotic CABG and conventional CABG, thus indicating that the surgical approach has a minimal impact and patient choice remains essential [34].

### 4.4 Pathophysiological Explanation

The pathophysiology of ischemic mitral regurgitation explains why different treatments have different outcomes. Pienta et al. (2023) explained that ischemic mitral regurgitation is a multifaceted condition that occurs after coronary artery disease and myocardial infarction due to impaired mitral valve leaflet function (tethering) and annular dilatation caused by ischemic ventricular remodeling [1]. As emphasised by Benfari et al. (2021), functional mitral regurgitation develops as a result of ventricular remodelling associated with left ventricular dysfunction and impaired valve coaptation in structurally normal mitral valves, This condition is associated with mechanisms such as left ventricular dilatation, papillary muscle dysfunction, and mitral annulus dilatation [2]. According to Russo et al. (2022), the main mechanism of functional mitral regurgitation is the displacement of the papillary muscles away from the mitral annulus due to ventricular enlargement, leading to apical/posterior tethering of the leaflets. in this process, loss of coaptation between the valve leaflets occurs, and annular dilatation and geometric distortions cause tenting (tenting) and loss of coaptation in the mitral valve [35]. As noted by Zoghbi et al. (2022), the pathophysiology of functional mitral regurgitation is based on an imbalance between valve leaflet tethering and reduced closing forces, and in ischemic cases, ventricular remodelling and tethering increase due to myocardial infarction, causing mitral regurgitation severity to form a 'biphasic' pattern in the early and late systolic phases [36]. Left ventricular mechanical dyssynchrony increases tethering through the incoordinated movement of the papillary muscles, while the dilation of the mitral annulus with left atrial dilatation and the 'atriogenic leaflet tethering' mechanism exacerbate functional mitral regurgitation. this pathophysiological understanding suggests that left ventricular reverse remodelling and load reduction may reduce functional mitral regurgitation [35]. The research by Ceresa et al. (2022) confirms that functional mitral regurgitation is mainly a ventricular disease and that intervention on the valve alone is not always necessary, suggesting that left ventricular remodelling and changes in mitral valve reserve may be sufficient in many patients with isolated CABG [23].

### 4.5 Compliance with Guideline Recommendations

Our current findings appear consistent with current guideline recommendations, According to Otto et al. (2021) the 2020 ACC/AHA Guidelines state that a heart team should make individualized decisions for patient with severe mitral regurgitation who remain symptomatic despite heart failure therapy particularly noting conflicting data on surgical outcomes in patients with secondary mitral regurgitation [7]. The ESC/EACTS guidelines according to Vahanian et al. (2021) emphasize the importance of selecting appropriate patients because COAPT and MITRA-FR studies have produced conflicting results which complicate clinical decision-making and generate inconsistencies in the literature [8]. Grant et al. (2024) stress the need for individualized decision-making and a multidisciplinary heart team in the Enhanced Recovery After Surgery consensus and state that a patient-centered approach is a key component of the treatment process. The study also points out the inconsistencies in surgical outcomes in patients with mitral insufficiency and the lack of consistency in treatment strategies across different risk groups [37]. Frazzetto et al. (2025) review that current guidelines recommend individualized treatment decisions and a multidisciplinary cardiac team approach and emphasize the need for patient specific decisions based on mechanism, surgical risk, and anatomical suitability [38]. As emphasized by Lopes et al. (2021), there are significant uncertainties in the diagnosis, risk stratification, and treatment decision-making processes for functional mitral insufficiency. differences in the threshold for severe regurgitation and treatment approaches in American and European guidelines create contradictions in clinical decisions, and it is noted that the prognosis of the disease depends not only on the severity of regurgitation but also on additional factors such as left ventricular remodelling and myocardial fibrosis [9]. The study by Vajapey and Kwon et al. (2021) and Guarracino et al. (2021) highlights that clinical practice inconsistencies occur because of different results from randomised studies and a patient-specific, multidisciplinary team-based approach is recommended for cardiac surgery patients [39,40].

### 4.6 Limitations

The research contains multiple crucial limitations that need to be addressed. The included studies show substantial heterogeneity because the I² value reached 51.42% in studies that recommend MVP. The heterogeneity exists because researchers employed different methodologies while working with patients who had different characteristics and used distinct surgical approaches. The observational nature of 66.7% of included studies increases both selection bias and confounding factor influence because they consisted of retrospective and prospective and cohort studies. The studies presented different follow-up durations which ranged from 17 months to 78 months thus making it challenging to compare long term results. Additionally, the fact that all studies recommending CABG were of Chinese origin introduces geographical bias and affects the generalisability of the results. The grading system for mitral regurgitation and surgical indication criteria were not standardized across studies which resulted in different patient selection.

### 4.7 Clinical Implications

The results of this meta-analysis provide important clinical guidance for surgical decision-making in patients with moderate ischemic mitral regurgitation and coronary artery disease. In terms of patient selection criteria, the combined CABG+MVP approach may be considered in patients with left ventricular ejection fraction <40%, young patients with low surgical risk, and patients with high myocardial viability; however, isolated CABG is a safer option in patients with advanced age, high comorbidity, and low EF (<25%). The surgical decision making process should be individualised by a multidisciplinary cardiac team based on a comprehensive assessment of factors such as the patient's age, left ventricular function, comorbidities, surgical risk, general performance status, symptom level, ventricular size, mitral annulus width, and myocardial viability. In the risk- benefit analysis, the advantages of the combined approach in reducing residual mitral regurgitation and improving functional capacity should be balanced against

the increased risk of early mortality, longer surgery duration, increased morbidity, and neurological complications; and considering that the long-term survival advantage has not been proven, isolated CABG should be considered an adequate and safe option in most patients.

## 5. Conclusion

The study is consistent with studies recommending both methods. The effect size of the six studies recommending the MVP method was calculated as 0.30. The effect size value of the six studies recommending CABG was calculated as 0.28. Although there was no significant difference in the results, the studies recommending the MVP method were found to have a stronger effect. The fact that the six studies recommending CABG were conducted in China, the low level of heterogeneity, the high sample size, and the low publication years indicate that this method should be considered. The effect size value of the six studies recommending the MVP method was calculated as 0.30. The effect size value of the n=6 studies recommending CABG was calculated as 0.28. Although there was not much difference in the results, it was seen that the studies recommending the MVP method had a stronger effect. In addition to the stronger results of the studies recommending the MVP method, the average publication time of around 6 years and the fact that the publications were conducted by different researchers in different countries take this method one step further.

However, there is no significant difference between the two methods in terms of effect size.

## Declarations:

### Ethics approval and consent to participate:

This study was approved by the Şişli Etfal Training and Research Hospital Clinical Research Ethics Committee (Decision No: 2828). The requirement for informed consent was waived by the ethics committee (if applicable).

### Consent for publication:

Not applicable.

### Authors' Contributions:

Melike Elif Teker Açıkel: Project conceptualization, study design, comprehensive literature search, data extraction, quality assessment, statistical analysis, interpretation of results, creation of figures and tables, drafting of the manuscript, and critical revision of the final version.

**Nazmi Alperen Gül:** Support in literature screening, data verification, contribution to methodological assessment, and review/editing of the manuscript.

**İsmail Koramaz:** Clinical expertise contribution, supervision of data interpretation, critical revision for important intellectual content, and final approval of the manuscript.

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### Conflicts of Interest:

The authors declare no conflicts of interest.

### Data availability:

Available upon reasonable request.

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