ORIGINAL ARTICLE

# Coronary artery bypass on survival in patients with moderate ischemic mitral regurgitation: meta-analysis

## *Derivación de la arteria coronaria en supervivencia de pacientes con insuficiencia valvular mitral isquémica moderada: un meta-análisis*

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## Abstract

**Objective**: *The objective of the study was to systematically evaluate the effect of coronary artery bypass grafting (CABG) or CABG combined with mitral valve surgery (cMVS) on post-operative survival in patients with moderate ischemic mitral valve regurgitation.* **Materials and methods:** *Databases including PubMed, Web of Science, COCHRANE LIBRARY, WanFang Data, and CNKI Data were searched from inception to January 2020. According to the inclusion criterion, relevant articles were screened. After that we extracted data, assessed quality, and performed meta-analysis using RevMan 5.2.* **Results:** *A total of 4 randomized controlled trial and 14 retrospective study involving 4476 patients were included in the study. The CABG group was 2278 and the cMVS group was 1698. The results of meta-analysis showed that compared with CABG group, there were no statistically significant differences in the recent mortality (odds ratio [OR] = 0.88, p = 0.62), 1-year survival (OR = 1.03, p = 0.82), 1-year survival (OR = 1.07, p = 0.62), and long-term survival (OR = 0.95, p = 0.61) of the cMVS group.* **Conclusion:** *Current evidence indicates that patients in the cMVS group did not benefit from CABG group in survival after surgery.*

***Keywords:*** *Ischemic mitral regurgitation. Coronary artery bypass grafting. Meta-analysis.*

## Resumen

**Objetivo**. *Evaluar sistemáticamente el efecto del injerto de derivación de la arteria coronaria (CABG) o el injerto de derivación de la arteria coronaria combinados con la cirugía de la válvula mitral (cMVS) sobre la supervivencia posoperatoria en pacientes con insuficiencia valvular mitral isquémica moderada.* **Material y métodos**. *Se realizaron búsquedas en bases de datos que incluyen Pubmed, Web of Science, COCHRANE LIBRARY, WanFang Data y CNKI Data desde el inicio hasta enero de 2020. De acuerdo con el criterio de inclusión, se seleccionaron los artículos relevantes. Después de eso, extrajimos los datos, evaluamos la calidad y realizamos el metanálisis con RevMan 5.2.* **Resultados**. *Se incluyó un total de 4 ensayos controlados aleatorios (ECA) y 14 estudios retrospectivos con 4476 pacientes. El grupo CABG fue 2278, el grupo cMVS fue 1698. Los resultados del metanálisis mostraron que, en comparación con el grupo CABG, no hubo diferencias estadísticamente significativas en la mortalidad reciente (OR = 0.88, p = 0.62), supervivencia a 1 año (OR = 1.03, p = 0.82), supervivencia a 1 año (OR = 1.07, p = 0.62) y supervivencia a largo plazo (OR = 0.95, p = 0.61) del grupo cMVS.* **Conclusión**. *La evidencia actual indica que los pacientes del grupo cMVS no se beneficiaron del grupo CABG en la supervivencia después de la cirugía.*

***Palabras clave:*** *Insuficiencia mitral isquémica. Cirugía de revascularización coronaria. Metaanálisis.*

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Date of reception: 20-04-2021
Date of acceptance: 06-07-2021
DOI: 10.24875/CIRU.21000357

Cir Cir. 2022;90(2):180-186
Contents available at PubMed
www.cirugiaycirujanos.com

# Introduction

Ischemic mitral regurgitation (IMR) is one of the common complications after myocardial infarction and an important factor leading to heart failure and death. At present, the surgical treatment of severe IMR has been clear, but it is still controversial whether surgical treatment should be performed in patients with moderate IMR. Relevant research results showed that the long-term survival rate of patients with IMR combined with surgery was low, the residual rate of mitral regurgitation, the recurrence rate of mitral regurgitation, and the incidence of postoperative adverse events were higher, so coronary artery bypass grafting (CABG) combined with mitral valve surgery was not recommended[1-3]. Hamouda et al. retrospective studies have found that CABG combined with valve surgery in IMR can significantly improve the cardiac function and prognosis[4] compared with CABG alone. At present, there are many studies on the choice of treatment for IMR, but the results are still not uniform. By searching the relevant literature at home and abroad, we meta analyzed the influence of CABG combined with mitral valve surgery (cMVS) on the survival rate of patients with IMR, and provided some reference for the selection of clinical treatment.

## Materials and methods

### *Retrieval strategy*

This study retrieves PubMed,Web of ScienceCOCHRANE LIBRARYWanFang Data, and CNKI Data databases with the English keywords include “IMR,” “Ischemic mitral insufficiency,” “coronary artery bypass,” “off-pump coronary artery bypass surgery,” “OPCABG,” and “CABG” and the Chinese keywords include “ischemic mitral insufficiency,” “IMR,” “CABG,” “CABG,” and “non-stop CABG.” The year restriction is limited to the establishment of the library to January 2020, as an example of PubMed, the search is shown in figure 1.

### *Permission and exclusion standard*

All patients included in the study were moderate mitral regurgitation or insufficiency caused by coronary heart disease, excluding mild and severe and excluded patients with rheumatic heart valve disease, congenital heart valve disease, infective endocarditis, and so on. All included studies had related follow-up results.

((((coronary artery bypass[Title/Abstract] OR off-pump coronary artery bypass surgery[Title/Abstract]) OR OPCABG[Title/Abstract]) OR CABG[Title/Abstract]) AND "humans"[MeSH Terms]) AND ((Ischemic mitral regurgitation[Title/Abstract] OR Ischemic mitral insufficiency[Title/Abstract]) AND "humans"[MeSH Terms]) AND "humans"[MeSH Terms]

**Figure 1.** *Meta-analysis results are represented by forest maps.*

### *Document extraction*

The literature was selected by two authors (Chen Shao-chien and Lu Jing), If there are different opinions, the two authors will decide whether to be selected after discussion. The included literature was divided into randomized controlled trials or retrospective cohort controlled studies. The extraction results included: ① literature information: author, country, publication time of the literature; ② literature type: randomized controlled study, retrospective cohort controlled study; ③ literature characteristics: sample size, sex, age; and ④ observation events: post-operative perioperative mortality, the survival rate of 1 year after operation, the survival rate of 1-3 years after operation, and the survival rate of more than 3 years after operation.

### *Statistical methods*

The Revman 5.2 software provided by Cochrane Collaboration Network was used for meta-analysis, and the confidence level was set as 95%. The heterogeneity of the effect value of each independent study was tested. If there was no statistical heterogeneity ($p > 0.1$), the fixed effect model was used; if there was statistical heterogeneity ($p \leq 0.1$), and the random effect model was used. The results of meta-analysis were represented by forest map.

## Results

### *Results and basic information of literature retrieval*

There are 1466 documents were initially retrieved, remove the irrelevant research, review and repetitive literature by reading the article title and abstract. Finally, 4 randomized controlled studies and 15 retrospective

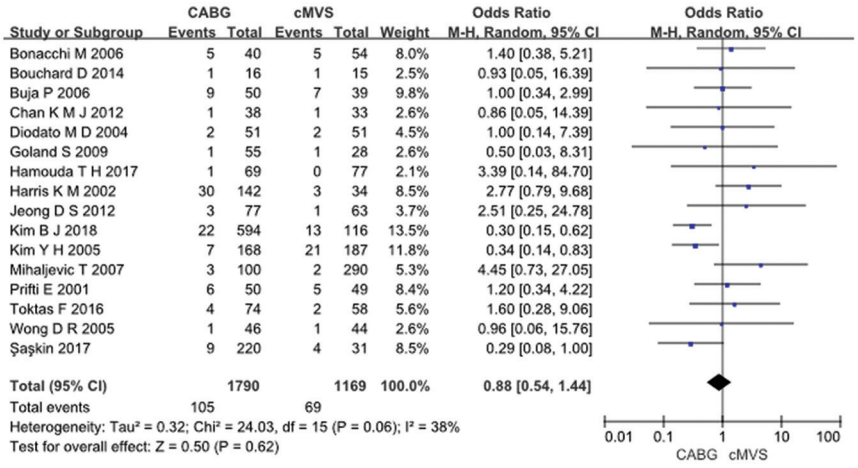


**Figure 2.** *Meta-analysis of post-operative perioperative mortality two groups.*

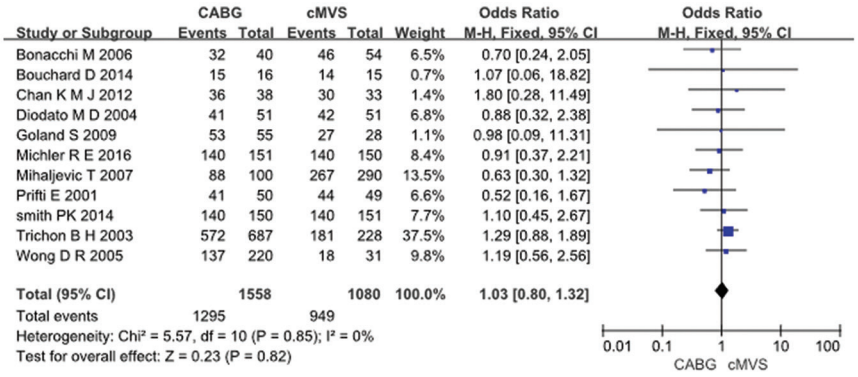


**Figure 3.** *Meta-analysis of 1-year survival after operation in two groups.*

controlled studies were included in the study from 2001 to 2018[2-20]. A total of 4476 patients were enrolled in this study, including 2778 patients in CABG group and 1698 patients in CMVs group. The baseline levels were compared between groups; there was no significant difference between the two groups. The basic information of the literature included is shown (Table 1).

## *Meta-analysis results*

### *Perioperative mortality*

The 16 studies[4-13,15-18,20] reported perioperative mortality after surgery, and the results showed statistical heterogeneity ($p = 0.06$, $I^2 = 38\%$), so the random effect model was used for meta-analysis. The results showed that there was no significant difference in perioperative mortality between CABG group and CMVs Group (odds ratio [OR] = 0.88, 95% confident interval [CI] [0.54, 1.44], p = 0.62) (Fig. 2).

### *1-year post-operative survival*

The 11 studies[3,5,6,8,9,14-16,19] reported the survival rate of 1 year after operation, and the results of each study were not statistically heterogeneous ($p = 0.85$, $I^2 = 0\%$), so the fixed effect model was used for meta-analysis. The results showed that there was no significant difference in 1-year survival rate between CABG group and CMVs Group (OR = 1.03, 95% CI [0.80, 1.32], p = 0.82) (Fig. 3).

### *1-3 years after surgery*

The 11 studies[5,9,14,16,17] reported the survival rate of 1-3 years after surgery, and the results of each study

**Table 1. Inclusion of basic literature**

| Author | Follow-up time (month) | Date of publication (year) | Country | Type of study | Age | | Sample size | | Observation of outcome |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | CABG | cMVS | CABG | cMVS | |
| Goland, 2009[2] | 61.2 ± 43.2 | 2009 | U.S. | Retrospective | 69 ± 11 | 68 ± 9 | 55 | 28 | ①、②、④ |
| Smith, 2014[3] | 12 | 2014 | U.S. | Randomized | 65.2 ± 11.3 | 64.3 ± 9.6 | 150 | 151 | ①、② |
| Hamouda, 2017[4] | 48 | 2017 | Arabia | Retrospective | 67 ± 7 | 63 ± 5 | 69 | 77 | ①、③ |
| Bonacchi, 2006[5] | 32 ± 11 | 2006 | Italy | Retrospective | 64.5 ± 6 | 64.6 ± 6 | 40 | 54 | ①、②、③、④ |
| Bouchard, 2014[6] | 12 | 2014 | Canada | Randomized | 65 ± 12 | 69 ± 7 | 16 | 15 | ①、② |
| Buja, 2006[7] | 34.9 ± 14.6 | 2006 | Italy | Retrospective | 75 ± 7.4 | 72 ± 9.1 | 50 | 39 | ①、②、④ |
| Chan, 2012[8] | 12 | 2012 | UK | Randomized | 70.4 ± 7.9 | 70.9 ± 10.5 | 38 | 33 | ①、② |
| Diodato, 2004[9] | 50 ± 20 | 2004 | U.S. | Retrospective | 69 ± 11 | 65 ± 10 | 51 | 51 | ①、②、③、④ |
| Harris, 2002[10] | 60 | 2002 | U.S. | Retrospective | 68.8 ± 9.8 | 65.6 ± 10.8 | 142 | 34 | ①、④ |
| Jeong, 2012[11] | 96 | 2012 | Korea | Retrospective | 65.4 ± 9.1 | 63.9 ± 9.1 | 77 | 63 | ①、④ |
| Kim, 2018[12] | 33.6–115.9 | 2018 | Korea | Retrospective | 65.2 ± 8.8 | 63.7 ± 9.4 | 594 | 116 | ①、④ |
| Kim, 2005[13] | 60 | 2005 | U.S. | Retrospective | 71 ± 11 | 72 ± 9 | 168 | 187 | ① |
| Michler, 2016[14] | 24 | 2016 | U.S. | Randomized | not described | | 151 | 150 | ②、③ |
| Mihaljevic, 2007[15] | 120 | 2007 | U.S. | Retrospective | 66 ± 9.2 | 66 ± 9.6 | 100 | 290 | ①、②、④ |
| Prifti, 2010[16] | 36 | 2001 | Italy | Retrospective | 64.5 ± 6 | 63.4 ± 5 | 50 | 49 | ①、②、③ |
| Şaşkin, 2017[17] | 51.3 ± 26.8 | 2017 | Turkey | Retrospective | 65.66 ± 9.95 | 64.1 ± 8.74 | 74 | 58 | ② |
| Toktas, 2016[18] | 17 | 2016 | Turkey | Retrospective | 63 ± 2.7 | 61 ± 3.2 | 46 | 44 | ① |
| Trichon, 2003[19] | 60 | 2003 | UK | Retrospective | 68（61，74） | 68（62，74） | 687 | 228 | ①、②、③、④ |
| Wong, 2005[20] | 12 | 2005 | U.S. | Retrospective | not described | | 220 | 31 | ①、② |

CABG: coronary artery bypass grafting, cMVS: coronary artery bypass grafting mitral valve surgery. ①Postoperative perioperative mortality, ②1-year survival, ③1-year survival, ④3-year survival greater than 3-year survival.

were not statistically heterogeneous (p = 0.41, $I^2$ =2%), so the fixed effect model was used for meta-analysis. The results showed that there was no significant difference in 1-3-year survival rate between CABG group and cMVS group (OR = 1.07, 95% CI [0.83, 1.37], p = 0.62) (Fig. 4).

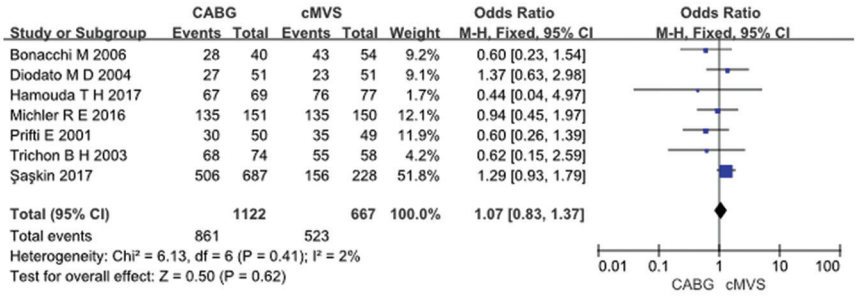


**Figure 4.** *Meta-analysis of 1-3-year survival rate between the two groups.*

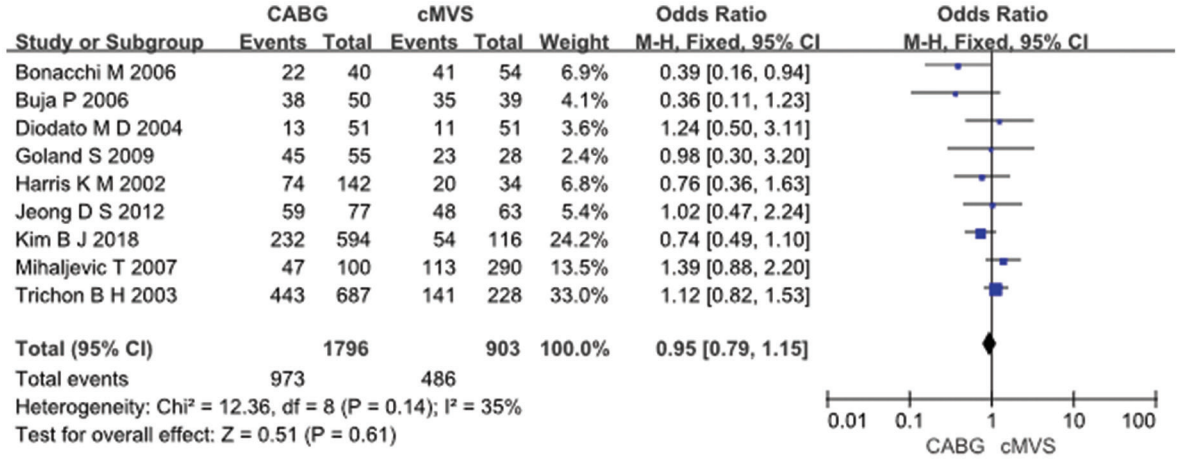


**Figure 5.** *Meta-analysis of survival rate greater than 3 years after operation in both groups.*

### *Postoperative survival rate greater than 3 years*

The 11 studies[5,7,9-12,15] reported the survival rate of more than 3 years after operation. and the studies of each study were not statistically heterogeneous ($p = 0.14$, $I^2 = 35\%$), so the fixed effect model was used for meta-analysis. The results showed that there was no significant difference in post-operative survival rate of more than 3 years between CABG group and cMVS group (OR = 0.95, 95%CI [0.79, 1.15], p = 0.61), (p = 0.61) (Fig. 5).

## Discussion

IMR is one of the common complications after ischemic heart disease and myocardial infarction caused by coronary atherosclerosis. It can be divided into acute and chronic IMR. The IMR is an important factor leading to heart failure and death. There were no typical pathological changes in the mitral lobe and subvalvular structure of IMR patients. Patients with acute IMR were mainly due to acute papillary muscle infarction and rupture, which causes increased left heart volume load and left heart function decompensation, which can lead to heart source Sexual shock. Chronic IMR patients are secondary to the phenomenon of left ventricular remodeling caused by local myocardial ischemia, resulting in the expansion and deformation of the mitral valve annulus, subvalvular structural displacement or traction, which are involved in the formation of IMR, so IMR is considered to be a function Sexual mitral regurgitation[21,22]. The current surgical treatment of IMR mainly includes three surgical methods: simple CABG, CABG combined with mitral valve replacement, and CABG combined with mitral valve repair. At present, there are many clinical studies on the choice of surgical methods for moderate IMR, but the post-operative effects of different surgical methods are still controversial.

The results of meta-analysis of this study showed that there was no significant difference in perioperative mortality, 1-year survival rate, 1-3-year survival rate, and

more than 3-year survival rate between the two groups compared with simple CABG, CMVs group had no obvious advantage in post-operative survival rate. Mallidi et al.[23] studies found that the perioperative risk of CMVs group was nearly 2 times higher than that of CABG alone. Complications caused by cardiopulmonary bypass cannot be avoided to a great extent with the development of CABG technology, especially the development and promotion of off-pump coronary artery bypass technology. Mallidi et al.[23] research found that the perioperative risk of cMVS group increased nearly 2 times compared with simple CABG. With the development of CABG, in particular, the development and promotion of CABG, complications due to cardiopulmonary bypass cannot be avoided to a great extent. Fatouch et al.[24] randomized controlled study results showed that CMVs group had more advantages in NYHA cardiac function classification and left ventricular diameter reduction, and mitral regurgitation was significantly improved in patients with postoperative mitral regurgitation. However, 40% of patients in CABG group had residual moderate to severe mitral regurgitation during long-term follow-up. Jeong et al.[11] found that for patients with IMR with a left ventricular ejection fraction <40%, cMVS can improve their postoperative residual mitral regurgitation, which is conducive to postoperative recovery and improves the quality of life, but its opening to exposed heart and longer turnaround time increase the risk of perioperative death. Kim et al.[12] found that cMVS increased the risk of early post-operative death and complications compared with simple CABG, and there seems to be no significant clinical benefit in long-term clinical and echocardiographic results.

Minghui et al.[25] suggested that individualized surgical scheme should be formulated for each patient, which is more favorable for the long-term prognosis of patients. For patients with multiple coronary artery disease, short life expectancy (< 5 years), and with large area of viable myocardium or normal papillary muscle function, simple CABG operation can be considered; for young patients with good pre-operative basic condition and stable condition, simple CABG can be considered, and CMVs should be considered actively.

The shortcomings of this study are as follows: (1) most of the references are retrospective controlled studies, which have some limitations. (2) The annual span of this study is large. Although the relevant literature is widely searched, there will still be unpublished literature and conference literature not included. Therefore, larger sample randomized controlled studies are needed to further verify this conclusion.

## Funding

The authors declare that this project was funded by the Zhejiang Provincial Health Commission Project (2018PY001).

## Conflicts of interest

The authors declare that they have no conflicts of interests.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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