



Research article

Percutaneous coronary intervention versus optimal medical therapy for stable coronary artery disease: An umbrella review

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ARTICLE INFO

Keywords:

Percutaneous coronary intervention
Optimal medical treatment
Stable Angina

ABSTRACT

Background: Invasive management of stable coronary artery disease is still a controversial topic. The purpose of this umbrella review was to synthesize systematic reviews (SRs) that evaluate the benefits and harms of percutaneous coronary intervention (PCI) versus optimal medical therapy (OMT) in patients with stable coronary artery disease.

Methods: We systematically searched PubMed/MEDLINE, Embase, and CENTRAL from 2018 to August 7, 2022. We included SRs with meta-analyses of randomized controlled trials (RCTs) that evaluated the question of interest. We assessed the methodological quality of the SRs with the AMSTAR-2 tool. We summarized the results of the outcomes for each SR. We calculated the degree of overlap of the RCTs included in the SRs using the corrected covered area (CCA).

Results: We found 10 SRs with meta-analyses. The SRs included 3 to 15 RCTs. The degree of overlap among the SRs was very high (CCA > 15%). No SR evaluated the certainty of the evidence using the GRADE system and 9 out of 10 had critically low methodological quality. The SRs reported heterogeneous results for the outcomes of all-cause mortality, myocardial infarction, revascularization, and angina. On the other hand, for the outcomes of cardiovascular mortality and stroke, all SRs agreed that there were no differences between PCI and OMT alone.

Conclusions: We found 10 SRs on the use of PCI compared to OMT alone for patients with stable coronary artery disease. However, none had high methodological quality, none evaluated the certainty of the evidence using the GRADE approach, and the results were inconsistent for several outcomes. This variability in evidence may result in divergent clinical decisions for the management of stable coronary artery disease among healthcare professionals. It is necessary to perform a high-quality SR using the GRADE approach to clarify the balance of benefits and harms of PCI.

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<https://doi.org/10.1016/j.heliyon.2024.e27210>

Received 14 June 2023; Received in revised form 11 November 2023; Accepted 26 February 2024

Available online 2 March 2024

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1. Background

Coronary artery disease is the accumulation of atherosclerotic plaque in the epicardial arteries. According to the World Health Organization, it is the leading cause of death worldwide, responsible for 16% of deaths [1]. This disease is dynamic and can present in a stable or unstable form. Stable coronary artery disease is characterized by the progressive accumulation of atherosclerotic plaque in the coronary arteries, while unstable disease typically occurs when there is a rupture or erosion of the plaque. Clinically, stable coronary artery disease presents as chest, neck, jaw, shoulder, or arm pain or discomfort, which typically occurs during physical exertion and is relieved by rest or nitrates within 5 min [2]. Elevated cholesterol levels, hypertension, smoking, diabetes, sedentary lifestyle, poor dietary choices, advanced age, and chronic inflammation are factors that can accelerate plaque build-up in the coronary arteries [3]. This accelerated plaque accumulation can cause an individual to progress from stable coronary artery disease to acute coronary syndrome.

The goal of treatment for stable coronary artery disease is to reduce the risk of cardiovascular complications and improve the quality of life of affected individuals. To achieve this goal, measures must be taken to modify lifestyle, such as following a healthy diet, exercising regularly, or quitting smoking. In addition, optimal medical therapy (OMT) should be used, which may include antithrombotics, hypolipidemics, angiotensin-converting enzyme inhibitors, beta-blockers, short-acting nitrates, and other medications [4]. Revascularization therapy is also available through percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG). PCI is a minimally invasive technique in which a stent is placed in the blocked artery to keep it open and improve blood flow. On the other hand, CABG is surgery that involves using a section of a patient's artery or vein or a donor's to create a bypass around the obstruction and restore blood flow. Revascularization is recommended in certain subgroups of patients with coronary artery disease who do not adequately respond to medical treatment, have a certain degree of obstruction in the coronary arteries, or have symptoms that limit their quality of life [5]. The choice between PCI and CABG depends mainly on the affected arteries, cardiac function and patient comorbidities [5].

Regarding the use of PCI for stable coronary artery disease, while systematic reviews (SRs) have been published, they present heterogeneous results among themselves [6,7]. This makes it difficult to evaluate the balance between potential benefits and harms. SRs often suffer from methodological limitations, particularly with regards to protocol registration, study selection, and data extraction [8]. The issue of low-quality SRs is not limited to any particular field and has also been observed in the field of cardiology. Even in high-impact journals, nearly 70% of SRs were found to exhibit low or critically low quality [9]. Umbrella reviews are a type of SR that seek to synthesize the information provided by other SRs, which can help improve understanding of the results and facilitate clinical decision-making. With this in mind, the present umbrella review aimed to synthesize SRs that evaluate the benefits and harms of PCI compared to OMT alone in patients with stable coronary artery disease. This review will allow us to select SRs that provide the most information on clinical outcomes, more recent searches, and a greater number of studies included. The results will help improve decision-making by healthcare professionals.

2. Methods

We followed the guidelines of the Preferred Reporting Items for Systematic and Meta-Analysis (PRISMA) 2020 (Additional file 1).

2.1. Eligibility criteria

We conducted an umbrella review. We included SRs with meta-analyses of randomized controlled trials (RCTs) published since 2018 that evaluated the benefits and harms of PCI compared to OMT alone in patients with stable coronary artery disease. We also included those SRs that evaluated more specific questions on the same topic. We did not include SRs without meta-analysis.

2.2. Literature search

We conducted a systematic search in PubMed/MEDLINE, Embase, and CENTRAL from January 1, 2018, to August 7, 2022. We chose this search period to find SRs that have included recent RCTs. We did not apply language restrictions. We grouped the main terms into two categories: "stable coronary artery disease" and "percutaneous coronary intervention". In addition, we applied search filters for SRs recommended by Cochrane adapted for each database [10]. The complete search strategy can be found in additional file 2.

2.3. Study selection

The records identified from the search strategy were imported into the Rayyan program where duplicate articles were removed. Two authors (AHCL and AGGU) independently reviewed the titles and abstracts of the articles and selected those potentially eligible. The selected studies were reviewed in full text by two authors (DFG and KGT) independently. Any discrepancies were resolved with a third author (DRSM). For those articles that were not available in full text, we intended to contact the authors by email.

2.4. Data extraction

Two authors independently (FCB and DFG) extracted the following data of interest from each article on a Microsoft Excel sheet: author, publication year, search date, number of meta-analyzed RCTs, details on the question (population, intervention, control group,

and evaluated outcomes), the tool used to assess the risk of bias, protocol registered in PROSPERO, results of the meta-analyses for each outcome of interest (number of studies, effect measure, point estimate, and confidence interval, I² heterogeneity), use of the GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) approach, and other analyses (subgroups, sensitivity, publication bias). In the case of an SR evaluating more than one question, we only extracted the studies from the meta-analysis that answered the question of interest. Any discrepancies were resolved with a third author (DRSM).

2.5. Risk of bias

For each SR, two authors (ANSM, DFG, AGGU, KGT) independently evaluated the methodological quality of the included articles using the AMSTAR-2 tool (A Measurement Tool to Assess systematic Reviews) [11]. This tool has 16 items of which 7 are critical. The rating of overall confidence can be high, moderate, low, or critically low depending on the number of critical and non-critical items met. In addition, we calculated the SR score, considering that each item that is met is one point, and adding these points.

2.6. Synthesis

We described the results of the reviews in tables and figures. In addition, we calculated the corrected covered area (CCA), a measure that allows evaluating the degree of overlap between the RCTs included by the SRs. The overlap can be low (0–5%), moderate (6–10%),

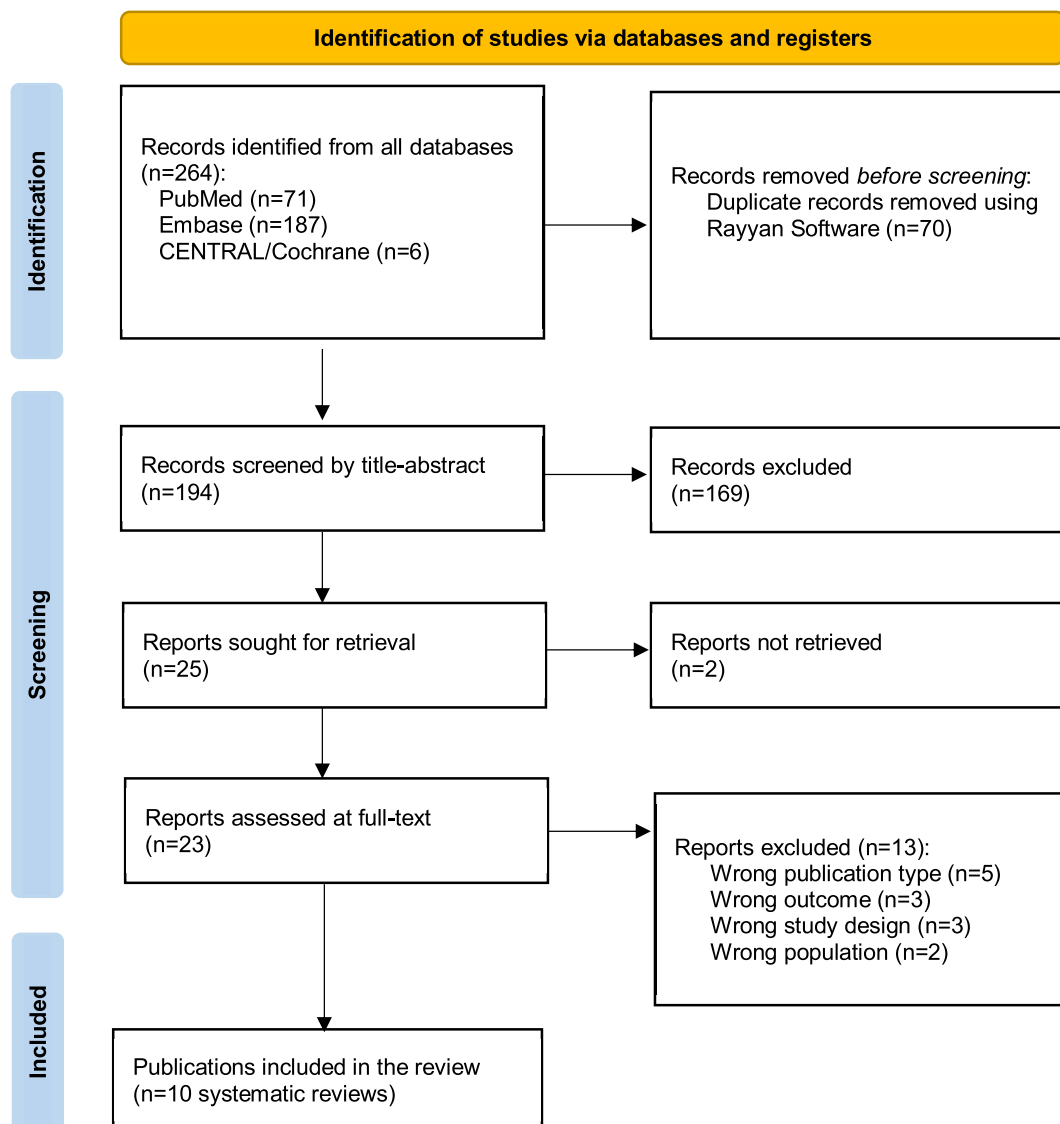


Fig. 1. Flow diagram summarizing the process of literature search and selection.

high (11–15%), or very high (>15%) [12].

3. Results

3.1. Study selection

After eliminating duplicate articles, we evaluated 194 records by title and abstract, of which 23 were reviewed in full text, and finally included 10 SRs with meta-analyses of RCTs [6,7,13–20] (Fig. 1). The reasons for the exclusion of the reviews evaluated in full text are in additional file 3.

3.2. Characteristics of the SRs

Of the 10 included SRs, 9 conducted their literature search between April 2018 and November 2021, and one did not mention its search period [15]. Only 2 SRs had a protocol registered in PROSPERO [13,18]. The number of meta-analyzed RCTs was 3–15. Seven SRs evaluated the risk of bias: 6 with the Cochrane tool [6,14,15,17–20] and 1 with the Jadad score [7,13]. None of the SRs used the GRADE approach to evaluate the certainty of the evidence. Eight SRs were self-funded and two reported receiving funding.

Out of the 10 SRs, 9 included patients with stable coronary artery disease, and one included patients with chronic total occlusion [6]. The intervention in 5 SRs was exclusively PCI, in 4 it was exclusively or predominantly PCI, and one study evaluated PCI guided by fractional flow reserve using second-generation drug-eluting stents [20].

Two SRs included studies that had a stent implantation rate of more than 50% in PCI and used statins in at least 50% of patients [13,16], the others did not specify other inclusion criteria. In all SRs, the comparator was OMT (Table 1). Most studies evaluated all-cause mortality and myocardial infarction as outcomes.

The 10 SRs included 37 RCTs [21–57], which are detailed in additional file 4. In general, we found that the CCA was 16.8%,

Table 1
Characteristics of systematic reviews included (n = 10).

Author (year)	Search period	Number of RCTs meta-analyzed	Population	Intervention	Control group	Risk of bias	Funding
Qian (2022) [6]	January 2010 to November 2021	12	Chronic total occlusion or significant coronary artery stenosis	Exclusively PCI	Optimal medical therapy	Cochrane Risk of Bias tool	National Natural Science Foundation of China and Soochow University Self-funded
Soares (2021) [13]	April 2020	7	Chronic coronary syndromes, obstructive coronary artery disease, and myocardial ischemia	Exclusively or predominantly with PCI	Optimal medical therapy	Jadad score	Self-funded
Chacko (2020) [14]	November 2019	15	Stable coronary artery disease	Exclusively or predominantly with PCI	Optimal medical therapy	Cochrane Risk of Bias tool	Self-funded
Shah (2022) [15]	NR	10	Chronic angina and stable coronary artery disease	Exclusively PCI	Optimal medical therapy	Cochrane Risk of Bias tool	Self-funded
Lerman (2021) [16]	January 2005 to 31 May 2020	6	Stable obstructive coronary artery disease	Exclusively PCI	Optimal medical therapy	No	Self-funded
Laukkanen (2021) [17]	November 2012 to 21 March 2020	11	Stable coronary artery disease	Exclusively PCI	Optimal medical therapy	Cochrane Risk of Bias tool	Self-funded
Davari (2022) [18]	December 2020	7	Stable coronary artery disease	Exclusively PCI	Optimal medical therapy	Cochrane Risk of Bias tool	Self-funded
Vij (2021) [19]	January 2000 to June 2020	7	Stable ischemic heart disease	Exclusively or predominantly with PCI	Optimal medical therapy	No	Self-funded
Zimmermann (2019) [20]	April 2018	3	Patients with stable coronary stenoses	Exclusively PCI guided by FFR using second-generation drug-eluting stents	Optimal medical therapy	Cochrane Risk of Bias tool	Canada Research Chairs Programme
Barbarawi (2021) [7]	May 2020	15	Stable coronary artery disease with significant stenosis	Exclusively or predominantly with PCI	Optimal medical therapy	No	Self-funded

RCT: randomized controlled trial; PCI: percutaneous coronary intervention; FFR: fractional flow reserve; NR: not reported.

indicating a very high degree of overlap (>15%) between the clinical RCTs included by the SRs. The degree of overlap between each SR is shown in Fig. 2.

3.3. Methodological quality assessment

When evaluating the methodological quality of the SRs with the AMSTAR-2 tool, we found scores between 5 and 13. Nine of the 10 SRs were rated as critically low methodological quality, except for the Davari-2022 study, which had low quality. None of the studies met the “source of funding of primary studies” item. In addition, 9 out of 10 SRs did not meet the “consideration of the risk of bias when interpreting the results of the review” item, and 8 out of 10 SRs did not meet the “impact of risk of bias of single studies on the results of the meta-analysis” item. The full evaluation is detailed in Table 2.

3.4. Comparison of the effect of PCI versus OMT alone on clinical outcomes

Of the 10 SRs with meta-analyses of RCTs, 9 evaluated the effect of PCI on all-cause mortality. Eight SRs found no significant differences between PCI and OMT, while one found that PCI decreased mortality compared to OMT [6]. Similarly, 8 SRs evaluated cardiovascular mortality and none found significant differences between PCI and OMT [7,14–20].

All of the included SRs evaluated myocardial infarction as an outcome. Three SRs found a statistically significant result indicating that PCI reduced the risk of developing myocardial infarction by 36%–14% compared to OMT [6,19,20]. However, heterogeneity was important in two of these SRs (I2 between 41% and 62%) [6,19] and the third SR did not report heterogeneity [20]. In addition, in 6 of the 7 SRs that did not find significant differences, the point effect value tended to decrease the risk of myocardial infarction [7,13–18] (Fig. 3).

The risk of stroke was evaluated in four SRs [6,17–19], but none found statistically significant differences between PCI and OMT (Fig. 3).

Five SRs evaluated revascularization as an outcome [6,7,15,17,18], of which 2 reported that the risk of PCI revascularization decreased significantly (by 42%–48%) compared to OMT [15,17] although with important heterogeneity (I2 between 79% and 93.8%) (Fig. 3).

In addition, 4 SRs evaluated angina as an outcome [7,15,17,18], of which two did not report statistically significant differences [17, 18], one reported a statistically significant reduction in angina (OR: 1.55; 95% CI: 1.14 to 2.10) [15] and one found a reduction in hospitalization for unstable angina (RR: 0.46; 95% CI: 0.32 to 0.67) [7]. On the other hand, only one SR reported that there were no statistically significant differences in the quality of life of those who were intervened with PCI versus OMT (MD = 10.44; 95% CI: –1.84 to 22.73) [6] additional file 5. No SR evaluated other safety outcomes between PCI and OMT.

3.5. Other analyses: publication bias, sensitivity, subgroups

Three studies evaluated publication bias with a funnel plot for all-cause mortality [6,7,14]. The included SRs performed the following subgroup analyses: 3 evaluated according to stent type [15,17,19], 2 according to diabetes [7,20], 1 according to publication date and type of PCI [17], and 1 according to age, sex, previous myocardial infarction, smoking, and fractional flow reserve status [20]. In addition, the SRs performed the following sensitivity analyses: 4 consecutively eliminated RCTs [7,13–15], 3 evaluated according to

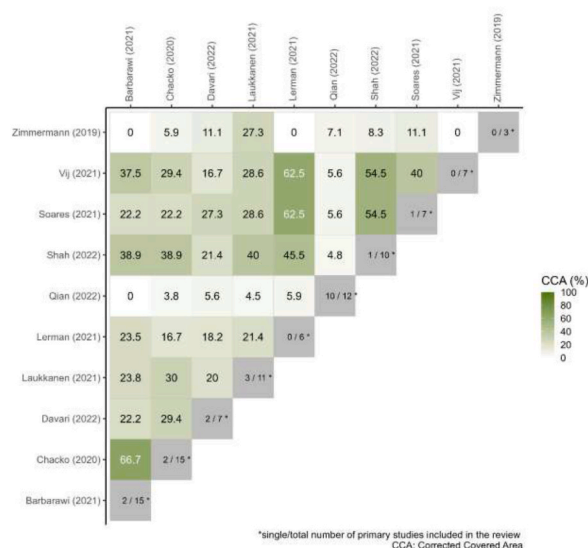


Fig. 2. Corrected covered area among the included systematic reviews.

Table 2
Methodological quality assessment using the AMSTAR-II tool.

Items	Qian (2022)	Soares (2021)	Chacko (2020)	Shah (2022)	Lerman (2021)	Laukkanen (2021)	Davari (2022)	Vij (2021)	Zimmermann (2019)	Barbarawi (2021)
1 PICO description	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2 Protocol registered before the commencement of the review	No	Yes	Yes	No	No	No	Yes	No	No	No
3 Study design included in the review	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No
4 Adequacy of the literature search	No	Yes	No	No	No	Yes	Yes	No	Yes	Yes
5 Two authors study selection	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes
6 Two authors study extraction	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes
7 Justification for excluding individual studies	No	No	No	Yes	No	No	Yes	No	Yes	No
8 Included studies described in detail	No	Yes	Yes	Yes	No	Yes	Yes	No	No	Yes
9 Risk of bias for the single studies being included in the review	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	No
10 Source of funding of primary studies	No	No	No	No	No	No	No	No	No	No
11 Appropriateness of meta-analytical methods	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
12 Impact of risk of bias of single studies on the results of the meta-analysis	No	No	Yes	No	No	No	No	No	No	Yes
13 Consideration of risk of bias when interpreting the results of the review	No	No	Yes	No	No	No	No	No	No	No
14 Explanation and discussion of the heterogeneity observed	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
15 Assessment of presence and likely impact of publication bias	No	No	Yes	No	No	Yes	Yes	No	No	No
16 Funding sources and conflict of interest declared	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Final score	6	9	13	9	7	8	13	5	10	9
Final rating	Critically low	Critically low	Critically low	Critically low	Critically low	Critically low	Low	Critically low	Critically low	Critically low

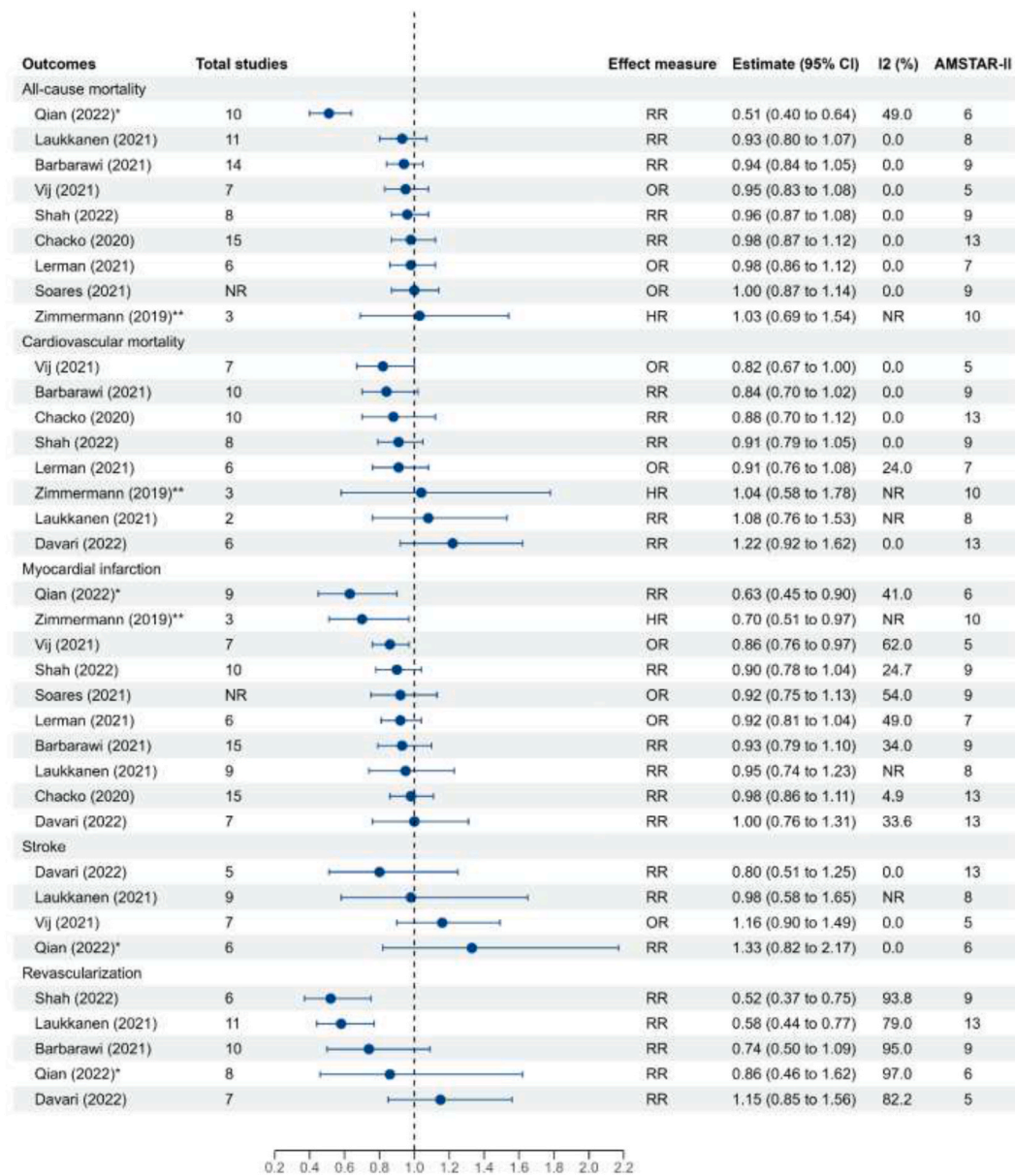


Fig. 3. Results of the included systematic reviews according to outcomes.

* Qian [6] includes studies in patients with chronic total coronary occlusion.** Zimmermann [20] only includes fractional flow reserve-guided PCI using secondgeneration drug-eluting stents as an intervention.

follow-up time [14,15,18], 1 according to sample size [15], 1 according to the type of allocation concealment and blinding of the results [17], 1 according to randomization time [20], 1 by including only nonprocedural myocardial infarction [7] and 1 according to the risk of bias and excluding CABG [14].

4. Discussion

This umbrella review included 10 SRs of RCTs that evaluated the effect of PCI compared to OMT in patients with stable angina. In general, all SRs evaluated a similar question, except for the study by Qian which included studies in patients with chronic total coronary occlusion, and the study by Zimmermann which only evaluated PCI intervention guided by fractional flow reserve using second-generation drug-eluting stents. We observed a very high degree of overlap among the SRs, signifying a notable redundancy in the literature, as multiple SRs with comparable research questions and incorporating similar articles have been published on this subject.

Regarding the results of the SRs, we found that meta-analyses show heterogeneous results for all-cause mortality, myocardial infarction, revascularization, and angina outcomes, a finding that is to be expected since each SR included different RCTs. The variability in RCT inclusion across SRs can also be attributed to the inherent complexities in the SR process, wherein authors face multiple decision points that may lead to the inclusion of different RCTs, even in high-quality SRs. These decision points encompass various factors, including the efficacy of search strategies, the clarity of inclusion criteria and protocols, challenges encountered during the selection process, limited availability of full-text articles, and, as identified in our analysis, variations in methodological quality according to the AMSTAR-2 assessment. In addition to heterogeneity between SRs, we also found significant heterogeneity in the meta-analyses (high I^2), particularly for myocardial infarction and revascularization outcomes. This heterogeneity may be due to the clinical and methodological variability of the included RCTs. The factors that could influence clinical variability are mainly the selection of the population of interest (disagreements in angiographic criteria for defining stable coronary artery disease), the type of intervention received (exclusively PCI or in combination with other therapies), and differences in the OMT received by each patient. In addition, it is important to note that the OMT may have changed according to the year of the trial due to new developments, however, we did not observe a clear tendency according to the year of publication of the SRs. The factors that could influence methodological heterogeneity are the risk of bias in each included study (mostly with a high risk of bias) and the methodological design (some without random sequence assignment and most without information about blinding). Also, it is imperative to recognize that even trials with identical initial methodologies may diverge in their enrolled patient populations. On the other hand, for cardiovascular mortality and stroke outcomes, all SRs agreed that there are no differences between the two treatments and that there is low statistical heterogeneity.

In order to make a decision on the use of an intervention, it is necessary to evaluate all possible critical and important outcomes of benefits and harms that have been established, including all-cause mortality, admissions (myocardial infarction, stroke, etc.), procedural interventions, acute renal failure, patient-reported outcomes (angina, depression, quality of life, etc.), and other adverse outcomes of importance related to the use of PCI (hospital stay, bleeding, etc.) [58]. However, most SRs only analyzed a limited number of outcomes, and none evaluated outcomes related to the use of PCI, except for stroke. Additionally, SRs must use the GRADE system to evaluate how much confidence is placed in the obtained results. The GRADE approach allows a systematic evaluation of the certainty of the evidence, meaning how much confidence is placed in the results obtained. It is a valuable tool for both researchers and clinicians, as it facilitates a clear understanding of the certainty of the results derived from SRs. The application of the GRADE methodology increases the credibility of the results, allowing stakeholders to make more informed, evidence-based decisions. However, we found that none of the SRs used this approach.

It is also important to consider that an SR should conduct planned subgroup analyses and meta-regression from the protocol to evaluate potential sources of heterogeneity, and sensitivity analyses to evaluate the consistency of the results. However, only a limited number of SRs conducted these types of analyses, and ideally authors should provide explanations regarding the selection of variables for these analyses. Future SRs should consider planning for groups of importance that may modify the association between successful PCI and patient outcomes, such as diabetes, multivessel disease, more severe disease, previous myocardial infarction, among others [59]. It is also important for SRs to evaluate publication bias through graphical and statistical methods.

In this context, we could choose the best SR based on certain criteria, but these have limitations. For example, one could choose the SR that includes the largest number of RCTs or the one with the most exhaustive bibliographic search and the most rigorous methodology, but these solutions may lead to the exclusion of the most recent studies, which is a significant limitation in an area where new studies are constantly being published. Another aspect to consider is the date of the SR. We found that the last SR was carried out by Quian et al. [6]; however, it was a study with critically low-reliability results. These approaches to selecting the SR with the best characteristics may lead to a loss of information, but this leads to better efficiency in the context of overproduction and allows for a simpler and more reliable result. In general, we recommend interpreting the results for each outcome and trusting SRs with the best methodological quality and the largest number of included studies. Furthermore, the heterogeneity found highlights the need for personalized treatment decisions in stable coronary artery disease, considering each patient's unique characteristics and requirements. Conflicting results and significant heterogeneity emphasize the complexity of this clinical field. Clinicians should weigh individual patient factors, comorbidities, and preferences when making treatment choices.

On the other hand, to enhance the quality of academic publications, it is advisable for publishers and researchers to refrain from publishing articles that closely resemble existing works as this may lead to greater use of human and economic resources. A possible solution to facilitate this is the publication of SR protocols in an international registry like PROSPERO. Another valuable perspective is that, given the numerous arbitrary decision-points involved in conducting SRs, it can be beneficial for multiple research groups to independently undertake SRs on the same topic. This approach allows for an examination of whether different groups arrive at the same conclusions and provides an opportunity for systematic overviews to elucidate the distinctions, strengths, and weaknesses of various approaches.

5. Strengths and limitations

This umbrella review has several strengths. We conducted a comprehensive systematic search in the main databases. We only included SRs with meta-analyses of RCTs. We independently carried out the selection, extraction, and analysis of the methodological quality of each study. In addition, our findings will be useful for planning future high-quality SRs [60]. However, the information provided by this work has some limitations. Most of the included SRs had methodological shortcomings, including lack of use of GRADE approach, lack of protocol registration, failure to report funding sources of included RCTs, and failure to consider the impact of risk of bias when interpreting results. We found that the SRs included different numbers of studies and found contradictory findings for some outcomes, even though most evaluated the same question.

6. Conclusion

In this umbrella review, we found 10 SRs of RCTs that compared PCI versus OMT alone for patients with stable coronary artery disease. We found that the CCA value was very high, indicating an overproduction of SRs on the topic. However, most of the SRs were of low methodological quality and had conflicting results for the outcomes of all-cause mortality, myocardial infarction, revascularization, and angina. On the other hand, all SRs found no differences in the outcomes of cardiovascular mortality and stroke. A high-quality SR on this topic that evaluates all important outcomes of benefits and harms and uses the GRADE approach to assess the certainty of the evidence is needed.

Ethics approval and consent to participate

Not applicable.

Funding

This umbrella review was self-funded.

Consent for publication

Not applicable.

Data availability statement

All data is included in the article or in the supplementary material.

CRedit authorship contribution statement

David R. Soriano-Moreno: Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Methodology, Investigation, Conceptualization. **Daniel Fernandez-Guzman:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Conceptualization. **Kimberly G. Tuco:** Writing – review & editing, Writing – original draft, Methodology, Investigation. **Anderson N. Soriano-Moreno:** Writing – review & editing, Writing – original draft, Methodology, Investigation. **Fabricio Ccami-Bernal:** Writing – review & editing, Writing – original draft, Methodology, Investigation. **Abdiel H. Coico-Lama:** Writing – review & editing, Writing – original draft, Methodology, Investigation. **Antony G. González-Uribe:** Writing – review & editing, Writing – original draft, Methodology, Investigation. **Alvaro Taype-Rondan:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

Not applicable.

List of abbreviations

SRs	systematic reviews
RCTs	randomized controlled trials
PCI	percutaneous coronary intervention
OMT	versus optimal medical therapy
CABG	coronary artery bypass graft
GRADE	Grading of Recommendations, Assessment, Development, and Evaluations
CCA	corrected covered area

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.heliyon.2024.e27210>.

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