The Heart Surgery Forum

*Heart Surg. Forum* **2026**; 29(6): 48626
https://doi.org/10.31083/HSF48626

*Systematic Review*

# Mid-Term and Long-Term Mortality Following Hybrid Coronary Revascularization Versus Off-Pump Coronary Artery Bypass Grafting: A Meta-Analysis

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Academic Editor: Gregory D. Trachiotis
Submitted: 28 November 2025 Revised: 21 March 2026 Accepted: 24 March 2026 Published: 23 June 2026

**Abstract**

**Background**: While numerous meta-analyses have explored the outcomes of various coronary revascularization strategies, the majority of existing literature predominantly concentrates on short-term results. Recognizing the limited focus on mid- and long-term outcomes, this meta-analysis aims to contribute to the understanding of the comparative effectiveness of hybrid coronary revascularization (HCR) and off-pump coronary artery bypass (OPCAB) procedures in these extended timeframes. **Methods**: A systematic literature review adhering to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines was conducted across multiple databases, including OVID MEDLINE®, EMBASE, SCOPUS, and PUBMED, up to January 2024. Inclusion criteria focused on studies reporting mid-term mortality (>1 year and <5 years) and/or long-term mortality (≥5 years) in patients undergoing HCR or OPCAB. Statistical analysis included hazard ratios (HRs) with 95% confidence intervals (CIs) using a random-effects model, assessment of heterogeneity with $I^2$ statistics, and publication bias evaluation via funnel plot asymmetry. **Results**: Nine studies reported mid-term mortality (>1 year and <5 years) and five studies reported long-term mortality (≥5 years), including a total of 10,729 patients. The demographic characteristics of the patients showed no significant differences between the two intervention groups. There was no significant difference in mid-term mortality (HR: 0.94, 95% CI: 0.79–1.13, $p$ = 0.52) and no significant difference in the long-term mortality (HR: 0.71, 95% CI: 0.41–1.23, $p$ = 0.22). **Conclusion**: HCR demonstrated comparable mid-term and long-term mortality to OPCAB, suggesting similar sustained clinical efficacy between the two interventions. These findings have potential implications for clinical decision-making in cardiovascular care. However, it is crucial to acknowledge the limitations of this study, including potential biases in the included studies and constraints in the available data. Further research is warranted to validate and refine these results, considering the dynamic landscape of cardiovascular care.

**Keywords:** hybrid coronary revascularization; long-term mortality; meta-analysis; mid-term mortality; off-pump coronary artery bypass grafting

## 1. Introduction

Existing meta-analyses comparing coronary revascularization strategies have largely focused on short-term outcomes [1,2,3], leaving uncertainty regarding their longer-term clinical impact [4,5]. These studies, while valuable, often overlook the critical insights that mid- and long-term data can provide. Short-term outcomes, such as immediate postoperative recovery and early complication rates, are undoubtedly important; however, they may not fully capture the potential benefits and drawbacks of different surgical approaches that manifest over extended periods. Hence, there is a growing recognition of the need to focus more on long-term survival, quality of life, and other enduring outcomes.

Hybrid coronary revascularisation (HCR), which combines percutaneous coronary intervention (PCI) with coronary artery bypass grafting (CABG), and off-pump coronary artery bypass grafting (OPCABG), performed without the use of a heart-lung machine, are two advanced techniques that promise different benefits [6]. In contemporary practice, both HCR and OPCAB are increasingly utilized, yet their comparative durability remains unclear. By looking beyond the immediate postoperative period, this meta-analysis seeks to provide a more comprehensive understanding of how these strategies impact mid-term and long-term mortality. The lasting value of these coronary revascularization strategies can be better assessed by focusing on mid-term and long-term mortality. This approach is especially pertinent given the increasing adoption of these techniques in clinical practice and their potential to improve long-term patient outcomes.

The objective of this meta-analysis is to evaluate the sustained clinical efficacy of HCR versus OPCABG beyond the short-term period by comparing the mid-term and long-term mortality.

## 2. Methods

### *2.1 Literature Search Strategy*

A systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations [7]. The databases searched included OVID MEDLINE®, EMBASE, SCOPUS, and PUBMED from their inception until January 2024. The following search terms were used in various combinations: "hybrid coronary revascularization", "off-pump coronary artery bypass", "HCR versus OPCAB", "long-term outcomes", "mid-term outcomes", and "coronary artery disease". The reference lists of relevant articles were also manually screened to identify additional eligible studies.

### *2.2 Eligibility Criteria*

Studies were included in the analysis if they met specific eligibility criteria. The study design had to be either a randomized controlled trial (RCT), a propensity-matched study, or an observational cohort study. The population examined consisted of adult patients undergoing either HCR or OPCAB. Additionally, studies were required to report mid-term mortality, defined as survival outcomes between one and five years, or long-term mortality, defined as survival beyond five years. Only studies published in English were considered for inclusion.

Conversely, studies were excluded if they solely reported short-term mortality occurring within 30 days of surgery. Case reports, reviews, editorials, and conference abstracts that did not provide primary data were omitted. Furthermore, studies that lacked sufficient data to compute hazard ratios (HRs) or confidence intervals (CIs) were also excluded from consideration.

### *2.3 Data Extraction and Critical Appraisal*

Two independent reviewers (MC, HB) screened all titles and abstracts to identify eligible studies. Full-text articles of relevant studies were retrieved and assessed for inclusion. Disagreements were resolved through consensus or consultation with a third reviewer (SGR).

The quality of included studies was assessed using the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) scale [8] for observational studies and the Cochrane Risk of Bias (RoB 2.0) tool for randomized studies [9].

The ROBINS-I addressed 7 domains, including confounding, participant selection, classification of interventions, deviations from intended intervention(s), missing data, measurement of outcomes, and reported results. Each domain was judged as "low", "moderate", "no information", "serious", or "critical" risk. We derived the overall risk of bias judgment from the highest classified domain, that is, if one domain was classified as high risk, this was deemed high risk overall.

RoB 2.0 evaluates five key domains: randomization process, deviations from intended interventions, missing outcome data, measurement of outcomes, and selection of reported results. Each domain was judged as having a "low risk", "some concerns", or "high risk" of bias. The overall risk of bias for each study was determined based on the highest domain rating, ensuring a systematic evaluation of study quality.

### *2.4 Statistical Analysis*

All statistical analyses were performed using Review Manager (RevMan) Version 5.4.1, developed by The Nordic Cochrane Centre in Copenhagen, Denmark. Hazard ratios (HRs) with 95% confidence intervals (CIs) were used as the primary effect measure to compare mid-term and long-term mortality between HCR and OPCAB. A random-effects model was employed to account for inter-study variability and provide more conservative estimates [10]. Statistical heterogeneity among studies was evaluated using Cochran's Q test and quantified with $I^2$ statistics. Heterogeneity levels were classified as low ($I^2 = 25\%–49\%$), moderate ($I^2 = 50\%–74\%$), and high ($I^2 \geq 75\%$) [11].

Although several included studies reported major adverse cardiac and cerebrovascular events (MACCE), a quantitative meta-analysis for this outcome was not performed. This was due to significant heterogeneity in the definition and reporting of MACCE across studies, with variability in the components included (e.g., myocardial infarction, stroke, repeat revascularization, and death) and differences in follow-up time points. Additionally, insufficient reporting of time-to-event data (hazard ratios) limited the ability to perform a robust pooled analysis.

### *2.5 Subgroup and Sensitivity Analyses*

To explore potential sources of heterogeneity and assess the robustness of the findings, predefined subgroup analyses were conducted for both mid-term and long-term outcomes. The included studies were stratified based on key variables to better understand the differences in results. First, studies were categorized as either prospective or retrospective to evaluate potential biases associated with study type. Additionally, statistical methods used in each study were analyzed separately, distinguishing between those employing propensity score matching (PSM), inverse probability of treatment weighting (IPTW), or non-matched cohorts to assess the impact of statistical adjustment techniques. Sex-based analysis was performed by stratifying studies according to the proportion of female participants, distinguishing those with more than 30% female patients from those with 30% or fewer to investigate whether sex-related differences influenced outcomes. Similarly, diabetes prevalence was examined by comparing studies in which more than 40% of participants were diabetic with those in which 40% or fewer had diabetes, assessing whether diabetes affected the relative efficacy of HCR versus OPCAB. Finally, the hybrid strategy timing was assessed by classifying studies into simultaneous HCR, where minimally invasive direct coronary artery bypass (MIDCAB) or robotic left internal mammary artery to left anterior descending artery (LIMA-LAD) bypass was combined with PCI in a single session, and staged HCR, where CABG was performed first, followed by PCI after a delay, to determine whether the timing of revascularization influenced mortality outcomes.

The pooled hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated for each subgroup, and heterogeneity was assessed using $I^2$ statistics. A $p$ value < 0.05 was considered statistically significant for all subgroup comparisons.

This structured subgroup analysis aimed to identify potential effect modifiers, improve the interpretation of findings, and provide clinically relevant insights into the comparative effectiveness of HCR versus OPCAB across different patient populations and procedural strategies.

Additionally, a sensitivity analysis was conducted using the leave-one-out method to assess whether excluding any single study significantly altered the pooled results. This analysis was performed only for outcomes with at least five studies.

Publication bias was assessed using funnel plot asymmetry.

## 3. Results

### 3.1 Quantity of Evidence

A total of 30 studies were identified through database searches. After removing duplicates and screening titles/abstracts, 28 full-text articles were reviewed. Of these, 14 studies [12,13,14,15,16,17,18,19,20,21,22,23,24,25] met the inclusion criteria and were included in the meta-analysis (Fig. 1).

The final dataset consisted of 14 studies, encompassing a total of 10,729 patients. Among them, 2065 patients underwent HCR, while 7832 received OPCAB. The mean follow-up duration ranged from 1.5 to 10 years. Nine studies reported mid-term mortality (>1 year and <5 years), while five studies reported long-term mortality (≥5 years). Tables 1 (Ref. [12,13,14,15,16,17,18,19,20]), 2 (Ref. [21,22,23,24,25]) provide detailed baseline characteristics of the included studies.

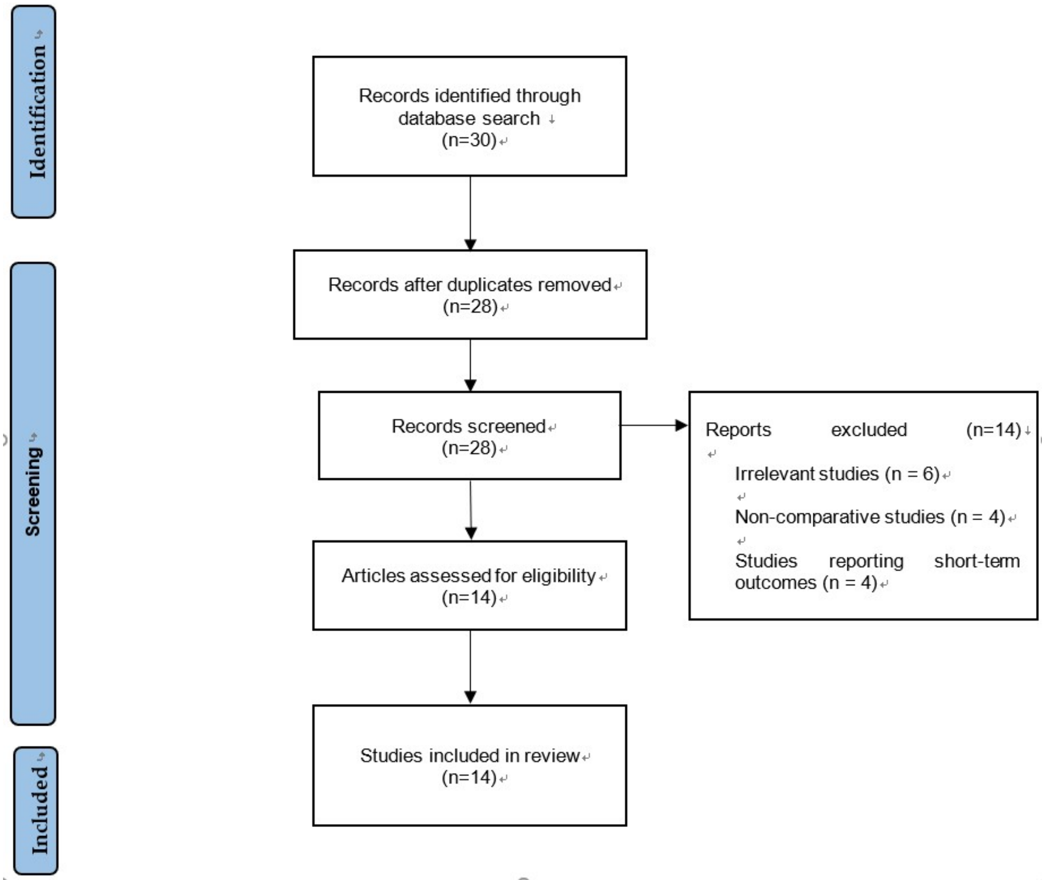


**Fig. 1. PRISMA flow diagram demonstrating assessment of the available literature.** PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

**Table 1. Characteristics of studies with mid-term follow-up.**

| Study | Design | Total sample size | HCR sample size | OPCAB sample size | Follow-up duration | Hybrid strategy | Mean age (years) | Female gender (%) | Diabetes (%) | Primary outcome | Secondary outcomes | Statistical analysis | Key findings |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hu et al. [12] 2011 | Propensity Score Matched | 208 | 104 | 104 | Mean 18 ± 7.9 months | HCR (MIDCAB + PCI) Simultaneous | 61.8 ± 10.2 | 10.6 | 25.0 | MACCE-free survival | ICU Stay, Blood Transfusion, Recovery Time | Kaplan-Meier, Cox Regression | HCR had shorter recovery time, lower MACCE rates than OPCAB |
| Halkos et al. [13] 2011 | Retrospective | 108 | 27 | 81 | Median 3.2 years | HCR (MIDCAB/Robotic + PCI) Staged. Interval: 2–3 days | 63.9 ± 13.7 | 48.2 | 29.6 | Survival, Repeat Revascularization | Blood Transfusion, Ventilation Time | Kaplan-Meier, Cox Regression | HCR had shorter ventilation times but higher revascularization rates than OPCAB |
| Halkos et al. [14] 2011 | Retrospective | 735 | 147 | 588 | Median 3.2 years | HCR (MIDCAB + PCI) Staged. Interval: NR | 64.3 ± 12.8 | 38.1 | 39.5 | Survival, MACCE, Revascularization | Blood Transfusion, ICU Stay | Kaplan-Meier, Cox Regression | HCR had similar survival but higher revascularization rates compared to OPCAB |
| Song et al. [15] 2016 | Propensity Score Matching 2:1 | 360 | 120 | 240 | Median 30.7 months | HCR (MIDCAB + PCI) Staged. Interval: NR | 62.3 ± 9.4 | 19.2 | 47.5 | MACCE | Stroke, Blood Transfusion, ICU Stay | Kaplan-Meier, Cox Regression | HCR had lower stroke rates and reduced perioperative invasiveness |
| Wu et al. [16] 2017 | Retrospective Cohort | 456 | 73 | 383 | Mean 25.0 ± 9.6 months | Two-Staged Hybrid (MIDCAB + PCI 5.3 ± 2.9 days post-surgery) | 61.1 ± 10.7 | 31.5 | 35.6 | MACCE, 3-Year Survival | Blood Loss, ICU Stay, Ventilation Time | Kaplan-Meier, Cox Regression | HCR showed reduced transfusion, shorter ICU stay, and similar survival to OPCAB |
| Vassiliades et al. [17] 2009 | Prospective Cohort | 4266 | 91 | 4175 | Mean 3 years | Staged, PCI within 48 h of CABG | 64.7 ± 13.7 | 33.0 | 40.7 | MACCE, 3-Year Survival | Reintervention Rate, Blood Transfusion | Cox Proportional Hazards | HCR showed noninferiority to OPCAB in MACCE and survival |
| Li et al. [18] 2021 | Propensity Matched Cohort | 302 | 151 | 151 | Median 20 months | One-Stop Hybrid | 64.6 ± 9.4 | 24.5 | 37.1 | MACCE | Blood Transfusion, ICU Stay, Length of Stay | Kaplan-Meier, Cox Regression | HCR had lower transfusion, shorter hospital stay, and similar MACCE rates to OPCAB |
| Harskamp et al. [19] 2015 | Propensity Matched Cohort | 1070 | 306 | 764 | Mean 3 years | Staged, robotic Interval: Median 3 days | 64.6 ± 11.6 | 29.7 | 36.9 | Survival, MACCE | Blood Transfusion, Hospital Stay | Kaplan-Meier, Cox Regression | HCR had shorter hospital stay and similar survival to OPCAB |
| Qiu et al. [20] 2019 | Propensity Matched Cohort | 94 | 47 | 47 | Mean 59 months | Staged, PCI after LIMA-LAD | 65.7 ± 8.8 | 13.5 | 44.2 | MACCE, Freedom from TVR | ICU Stay, Hospital Stay | Kaplan-Meier, Cox Regression | HCR had similar MACCE rates to OPCAB but lower TVR rates than PCI |

HCR, Hybrid Coronary Revascularization; ICU, Intensive Care Unit; LAD, Left Anterior Descending Artery; LIMA, Left Internal Mammary Artery; MACCE, Major Adverse Cardiac and Cerebrovascular Events; MIDCAB, Minimally Invasive Direct Coronary Artery Bypass; MI, Myocardial Infarction; NR, Not Reported; OPCAB, Off-Pump Coronary Artery Bypass; PCI, Percutaneous Coronary Intervention; CABG, coronary artery bypass grafting; TVR, target vessel revascularization.

**Table 2. Characteristics of studies with long-term follow-up.**

| Study | Design | Total sample size | HCR sample size | OPCAB sample size | Follow-up duration | Hybrid strategy | Mean age (years) | Female gender (%) | Diabetes (%) | Primary outcome | Secondary outcomes | Statistical analysis | Key findings |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hage et al. [21] 2019 | IPTW | 363 | 147 | 216 | Median 81–96 months | HCR (Robotic LIMA-LAD + PCI) 77.5% simultaneous | 64.3 ± 9.7 | 28.4 | 38.7 | Survival, Freedom from Revascularization, Angina | Perioperative complications, Hospital Stay, Bleeding | Kaplan-Meier, Cox Regression | HCR had shorter recovery, similar long-term outcomes as OPCAB, better freedom from angina |
| Basman et al. [22] 2020 | Propensity Matched Analysis | 200 | 100 | 100 | 8 Years | HCR (Robotic LIMA-LAD + PCI) staged. Interval: 4–6 weeks | 62.1 ± 10.3 | 23.2 | 42.5 | All-Cause Mortality | Repeat Revascularization, MACCE | Logistic Regression, Cox Proportional Hazards | No significant survival difference between HCR, CABG, and PCI; HCR had lower residual SYNTAX score than PCI |
| Torregrossa et al. [23] 2022 | Propensity Matched Analysis | 62 | 31 | 31 | Mean 7.0 ± 4.9 years | HCR (Robotic LIMA-LAD + PCI) simultaneous | 63.7 ± 9.1 | 100 | 38.5 | Survival, MACCE, Angina-Free Survival | Blood transfusion, Hospital Stay | Kaplan-Meier, Cox Regression | No significant difference in survival or MI; lower blood transfusion and hospital stay in HCR group |
| Torregrossa et al. [24] 2022 | IPTW | 731 | 181 | 412 | Mean 7.6 ± 4.8 years | HCR (Robotic LIMA-LAD + PCI) simultaneous | 73.8 ± 11.2 | 100 | 53 | Long-term Survival, MACCE | Blood transfusion, AF, ICU/Hospital Stay | IPTW-weighted Regression Models | HCR showed improved perioperative outcomes with similar long-term survival compared to OPCAB and ONCAB |
| Ding et al. [25] 2023 | Propensity Score Matched | 1620 | 540 | 540 | 10 Years | HCR (MIDCAB + PCI) Simultaneous | 61.3 ± 9.9 | 17.8 | 29.8 | MACCE, Functional Status | EuroSCORE II Strata Analysis | Kaplan-Meier, Cox Regression | HCR performed similarly to OPCAB but outperformed PCI in MACCE reduction |

HCR, Hybrid Coronary Revascularization; ICU, Intensive Care Unit; IPTW, Inverse Probability of Treatment Weighting; LAD, Left Anterior Descending Artery; LIMA, Left Internal Mammary Artery; MACCE, Major Adverse Cardiac and Cerebrovascular Events; MIDCAB, Minimally Invasive Direct Coronary Artery Bypass; MI, Myocardial Infarction; OPCAB, Off-Pump Coronary Artery Bypass; PCI, Percutaneous Coronary Intervention; SYNTAX Score, Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery Score (a measure of coronary lesion complexity); AF, atrial fibrillation; ONCAB, on-pump coronary artery bypass.

*3.2 Quality of Evidence*

The included studies comprised 14 observational cohort studies, of which two were prospective and ten were retrospective. Among the retrospective studies, six used propensity score matching (PSM), and two applied inverse probability of treatment weighting (IPTW). The included studies were assessed using the ROBINS-I tool to determine the risk of bias (**Supplementary Tables 1,2**). Most studies had moderate risk of bias, primarily due to residual confounding (non-random treatment allocation; incomplete adjustment for anatomic complexity such as Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery Score (a measure of coronary lesion complexity) [SYNTAX score]), classification of interventions (heterogeneity in staged vs simultaneous hybrid strategies and variability in minimally invasive techniques), and occasional concerns related to missing data and selective reporting of adjusted time-to-event estimates. While PSM and IPTW were used in several studies to adjust for confounders, factors such as SYNTAX score, lesion complexity, and operator expertise were not uniformly reported, introducing potential sources of bias.

*3.3 Basic Demographics*

3.3.1 Mid-Term Follow-Up Studies

A total of 9 studies with 7599 patients were included in the mid-term follow-up analysis [12,13,14,15,16,17,18,19,20]. Among them, 1066 patients underwent HCR, while 6533 patients received OPCAB. The weighted mean age of patients was 64.2 years. The proportion of female patients across these studies was 31.3%, and the prevalence of diabetes was 39.3%.

3.3.2 Long-Term Follow-Up Studies

A total of 5 studies with 2976 patients were included in the long-term follow-up analysis [21,22,23,24,25]. Among them, 999 patients underwent HCR, while 1299 patients received OPCAB. The weighted mean age of patients was 64.8 years. The proportion of female patients was 41.4%, and the prevalence of diabetes was 37.6%.

*3.4 Assessment of Study Endpoints*

3.4.1 Mid-Term Mortality

A total of 9 studies comprising 7599 participants reported mid-term mortality (>1 year and <5 years) [12,13,14,15,16,17,18,19,20]. The pooled HR for mid-term mortality comparing HCR and OPCAB was 0.94 (95% CI: 0.79–1.13, $p$ = 0.52) (Fig. 2), indicating no significant difference between the two strategies. Statistical heterogeneity was low ($I^2$ = 0%), suggesting consistency among included studies.

3.4.2 Long-Term Mortality

A total of 5 studies including 2976 participants reported long-term mortality (≥5 years) [21,22,23,24,25]. The pooled hazard ratio for long-term mortality was 0.71 (95% CI: 0.41–1.23, $p$ = 0.22) (Fig. 3), demonstrating no statistically significant difference in long-term survival between HCR and OPCAB. Heterogeneity was moderate to substantial ($I^2$ = 55%), suggesting that there is some variability among the included studies. This may be due to differences in study design, patient populations, follow-up duration, or procedural techniques across the studies. Despite this, the overall trend indicates comparable long-term survival outcomes between the two revascularization strategies.

3.4.3 Subgroup Analysis

Subgroup analyses for mid-term mortality included nine studies comprising 7599 participants (**Supplementary Table 3**). When stratified by study design, prospective studies suggested a non-significant trend favouring HCR compared with OPCAB (HR 0.23, 95% CI 0.04–1.17; $p$ = 0.08), whereas retrospective studies showed no difference between strategies (HR 0.96, 95% CI 0.89–1.15; $p$ = 0.65). Similarly, studies using propensity score matching demonstrated comparable outcomes between HCR and OPCAB (HR 1.01, 95% CI 0.83–1.24; $p$ = 0.89), while non-matched cohorts showed a non-significant trend toward improved survival with HCR (HR 0.74, 95% CI 0.51–1.07; $p$ = 0.11).

With respect to hybrid strategy timing, staged HCR was associated with outcomes similar to OPCAB (HR 0.95, 95% CI 0.79–1.13; $p$ = 0.55). In contrast, simultaneous HCR demonstrated a highly imprecise estimate with very wide confidence intervals (HR 0.33, 95% CI 0.01–8.19; $p$ = 0.50), reflecting the small number of included patients; this finding should therefore be interpreted with caution.

For long-term mortality, five retrospective studies including 2976 participants were analysed (**Supplementary Table 4**). The pooled estimate showed no significant difference between HCR and OPCAB (HR 0.71, 95% CI 0.41–1.23; $p$ = 0.22). Subgroup analyses by statistical methodology revealed no difference in propensity score-matched studies (HR 1.00, 95% CI 0.81–1.24; $p$ = 0.98), while IPTW-adjusted studies showed a non-significant trend favouring HCR (HR 0.47, 95% CI 0.12–1.85; $p$ = 0.28) with substantial heterogeneity. Analyses stratified by sex distribution, diabetes prevalence, and hybrid strategy timing did not demonstrate a consistent or statistically significant effect modification, with wide confidence intervals observed in several subgroups.

Overall, subgroup analyses did not identify a robust modifier of the association between revascularization strategy and mid- or long-term mortality, and findings from smaller subgroups should be considered hypothesis-generating.

*3.5 Sensitivity Analysis*

Sensitivity analyses, using a leave-one-out analysis, did not significantly alter the results (**Supplementary Ta-**

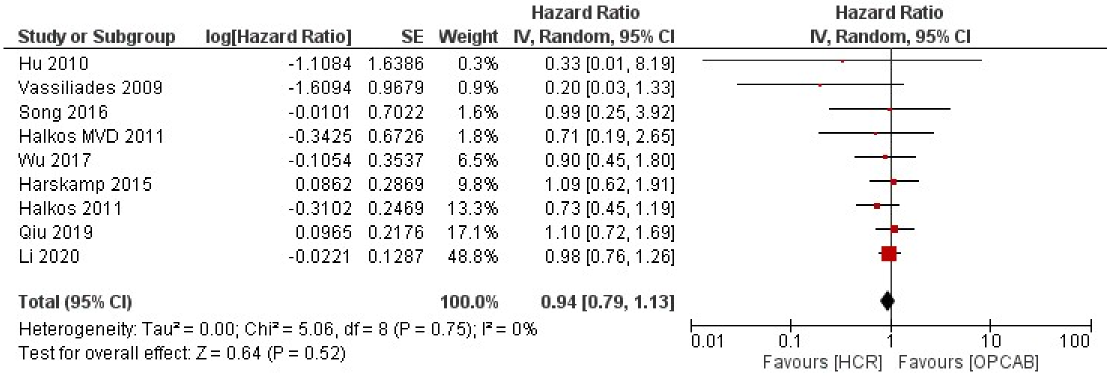


**Fig. 2. Forest plot for mid-term mortality comparing hybrid coronary revascularization and off-pump coronary artery bypass grafting.** SE, standard error; CI, confidence interval.

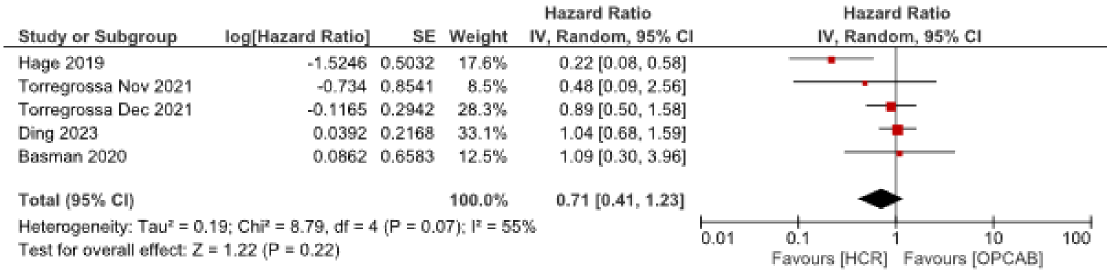


**Fig. 3. Forest plot for long-term mortality comparing hybrid coronary revascularization and off-pump coronary artery bypass grafting.**

**ble 5**). The overall effect sizes and 95% CIs remained largely consistent across all iterations, without any notable changes in the mid-term or long-term mortality analyses.

*3.6 Publication Bias*

Visual inspection of the funnel plots for both mid-term and long-term mortality analyses suggested potential publication bias, with asymmetry in the lower left region of both plots, indicating a lack of small studies with non-significant results (**Supplementary Figs. 1,2**). This suggests that negative or null findings may be underreported. While the possibility of bias cannot be ruled out, the overall findings remain robust, supporting comparable mid-term and long-term survival between HCR and OPCAB.

## 4. Discussion

This comprehensive meta-analysis directly comparing HCR and OPCABG reports similar mid-term and long-term mortality following HCR and OPCABG. The results of this meta-analysis confirm that both HCR and OPCAB are viable options for revascularisation of patients with multivessel coronary artery disease (CAD). The subgroup analysis did not identify any specific patient or procedural characteristic that significantly altered the comparative effectiveness of HCR and OPCAB in terms of mid-term or long-term mortality. While some subgroups suggested trends favouring HCR, none reached statistical significance. Notably, prospective studies suggested a potential benefit for HCR in mid-term mortality, but the small number of such studies limited statistical power. Similarly, simultaneous HCR showed a non-significant trend toward improved long-term survival, though moderate heterogeneity was present.

A plausible explanation for the comparable long-term mortality is that both strategies commonly rely on a LIMA–LAD graft, which provides excellent long-term patency and is a major determinant of durable survival benefit in multivessel CAD. When LAD revascularization is effectively achieved with LIMA-LAD in both approaches, incremental differences attributable to non-LAD targets treated by PCI (in HCR) versus additional surgical grafts (in OPCAB) may have a smaller impact on all-cause mortality over long follow-up, even if they influence recovery profiles or repeat revascularization.

HCR offers several advantages over traditional on-pump CABG. HCR combines the benefits of minimally invasive surgery with the efficacy of percutaneous coronary intervention (PCI), resulting in shorter hospital stay and quicker recovery time. This approach is particularly beneficial for patients with multivessel CAD, as it allows for complete revascularization with the "best of both worlds" from surgery (internal mammary artery anastomosis in less invasive fashion) and PCI (least invasive approach) [26]. In contrast, OPCABG, while avoiding the use of a heart-lung machine, requires a more invasive surgical approach and longer recovery period. However, OPCABG remains a valuable option for patients who may not be suitable candidates for HCR due to anatomical considerations or other factors [21]. Both techniques have shown excellent short-term outcomes, making them attractive alternative options for conventional on-pump CABG for patients with multivessel CAD.

The only previously published meta-analysis of 5 studies by Dong et al. [27], comparing mid-term mortality following HCR versus OPCAB, reported no significant difference in mid-term mortality between the two groups (RR: 0.47, 95% CI: 0.17–1.32, $p < 0.01$, P for heterogeneity = 0.34, $I^2 = 7\%$) similar to the findings of this updated meta-analysis of 9 studies (HR 0.94, 95% CI: 0.79–1.13, $p = 0.52$). To the best of our knowledge, this is the first meta-analysis comparing the long-term clinical mortality between HCR and OPCABG so far and reports comparable long-term mortality after HCR and OPCABG (HR 0.71, 95% CI: 0.41–1.23, $p = 0.22$). Despite the encouraging results reported by this meta-analysis and the well-recognised advantages of HCR and OPCABG, both these strategies have not yet been widely adopted by the surgical community. There are several reasons for this lack of universal adoption. Firstly, both techniques require a high level of surgical expertise and experience, which limits their availability to specialized centers. The learning curve for these procedures can be steep, and not all surgeons are trained or comfortable performing them [28]. Additionally, there is a lack of large-scale, long-term randomized controlled trials that conclusively demonstrate their superiority over conventional methods. This uncertainty makes some clinicians hesitant to adopt these newer techniques. Finally, logistical challenges, such as the need for specialized equipment and the coordination of multidisciplinary teams, can also be barriers to widespread adoption [15].

The significance of this meta-analysis lies in its potential to influence clinical decision-making and policy formulation. By highlighting mid- and long-term results, the study could inform best practices and guidelines for coronary revascularization, ultimately benefiting patients by aligning treatment strategies with their long-term health prospects. Moreover, this research underscores the importance of continuous innovation and assessment in medical procedures, ensuring that the evolving landscape of cardiac care is guided by robust and comprehensive evidence. Through this work, we aim to contribute valuable insights that enhance the quality and efficacy of coronary revascularization treatments.

Despite the aforementioned significance, this meta-analysis faces several limitations. The included studies are all observational in nature. Observational studies are inherently prone to biases, such as selection bias and confounding factors, which can distort the true effect of the interventions being compared. Additionally, the heterogeneity among the included studies—stemming from variations in patient populations, surgical techniques, and follow-up periods—can complicate the synthesis of results and reduce the reliability of the conclusions drawn [29]. Limitations also include heterogeneity in hybrid protocols (simultaneous vs staged and variable PCI–surgery intervals), differences in minimally invasive approaches (robotic TECAB/robotic LIMA–LAD vs MIDCAB), and inconsistent reporting of anatomic complexity (e.g., SYNTAX score), which may contribute to residual confounding despite statistical adjustment. Without the rigorous control of variables present in randomized controlled trials (RCTs), the findings of such a meta-analysis may lack the robustness needed to inform clinical practice decisively. A further limitation of this meta-analysis is the inability to perform a pooled analysis of MACCE. Although this outcome was reported in several included studies, substantial heterogeneity in its definition, inconsistent reporting of individual components, and lack of standardized time-to-event estimates precluded formal meta-analysis. As a result, conclusions regarding composite cardiovascular outcomes remain descriptive rather than quantitative. Consequently, while valuable, the results must be interpreted with caution and ideally supplemented with data from RCTs to provide a more comprehensive understanding of the comparative effectiveness of HCR and OPCAB.

## 5. Conclusion

In conclusion, this meta-analysis of observational studies comparing HCR versus OPCABG reveals similar mid-term and long-term mortality outcomes, highlighting the potential effectiveness of both procedures in ensuring patient survival over extended periods. For clinical practice, this analysis underscores the importance of individualized patient assessment and the consideration of each technique's specific advantages. To provide more definitive guidance and strengthen the evidence base, RCTs are imperative. These trials would offer more robust data, minimize biases, and clarify the comparative benefits and risks of HCR and OPCABG, ultimately guiding more precise and informed clinical decision-making.

## Availability of Data and Materials

The datasets analyzed during the current study are available from the corresponding author upon reasonable request.

## Author Contributions

MC contributed to study conception and design, literature search, data extraction, statistical analysis, interpretation of results, and manuscript drafting. HB contributed to data interpretation, critical revision of the manuscript, and intellectual content. SGR supervised the study, contributed to the study design, interpretation of findings, and critical revision of the manuscript. All authors reviewed and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

## Ethics Approval and Consent to Participate

Not applicable.


## Acknowledgment

Not applicable.

## Funding

This research received no external funding.


## Conflicts of Interest

The authors declare no conflict of interest.

## Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/HSF48626.

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