

# On-Pump versus Off-Pump Coronary Artery Bypass Grafting: A Meta-Analysis

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#### **ABSTRACT**

**Background:** Coronary artery disease (CAD) remains a leading global cause of mortality and morbidity. While both on-pump and off-pump coronary artery bypass grafting (CABG) are used for surgical revascularization, the optimal approach remains debated. On-pump CABG, involving cardiopulmonary bypass (CPB), offers a motionless surgical field but is associated with systemic complications. Off-pump CABG avoids CPB, potentially reducing inflammation, neurocognitive damage, and renal dysfunction, particularly in high-risk patients. However, concerns about incomplete revascularization and long-term graft patency persist.

**Objective:** This meta-analysis aimed to compare clinical outcomes between on-pump and off-pump CABG using data from randomized controlled trials (RCTs) to provide statistically significant evidence.

**Methods:** A systematic search of PubMed, Cochrane Library, Embase, Scopus, and Google Scholar identified eligible RCTs. Studies reporting risk ratios (RRs) and odds ratios (ORs) for clinical outcomes were included. Statistical analyses were conducted using Stata-16 with a random-effects model. Heterogeneity and publication bias were assessed.

**Results:** Seven RCTs were analyzed. The pooled RR for off-pump versus on-pump CABG was 0.93 (95% CI: 0.78–1.07), and the pooled OR was 0.92 (95% CI: 0.75–1.10), indicating no statistically significant difference. Heterogeneity was low to moderate ( $I^2 \approx 30\%$ ). Funnel plot inspection showed minimal publication bias.

**Conclusion:** Off-pump CABG demonstrated a slight, non-significant reduction in adverse outcomes compared to on-pump CABG. Both approaches appear comparable in safety and effectiveness. Surgical expertise and patient selection remain crucial in determining the optimal technique.

Keywords: Coronary Artery Bypass Grafting; On-Pump CABG; Off-pump CABG

## 1. INTRODUCTION

Coronary artery disease (CAD) continues to be a primary cause of death and morbidity worldwide, significantly impacting individual health outcomes and healthcare systems. Coronary artery disease (CAD) is defined by the constriction or total occlusion of coronary arteries caused by the accumulation of atherosclerotic plaques, potentially leading to myocardial ischaemia, angina pectoris, heart failure, and acute coronary syndromes, including myocardial infarction. Although medical therapy and percutaneous coronary interventions (PCI) are essential in managing coronary artery disease (CAD), especially in early or less severe cases, surgical revascularisation via coronary artery bypass grafting (CABG) remains the gold standard for patients with multivessel disease, left main coronary artery involvement, or diabetes mellitus. It is especially favoured in instances requiring comprehensive and lasting revascularisation.<sup>1</sup>

Conventionally, coronary artery bypass grafting has been done with cardiopulmonary bypass (CPB), known as on-pump CABG, during which the heart is halted by cardioplegia, and a mechanical pump temporarily assumes the roles of the heart and lungs. This provides the surgeon with a stable, bloodless operational area, facilitating accurate anastomosis of bypass grafts. The use of CPB is linked to a series of systemic consequences, encompassing an intensified inflammatory response, neurocognitive impairment, renal dysfunction, coagulation irregularities, and an elevated chance of stroke, especially in older

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or high-risk individuals. The difficulties mostly arise from artificial circulation and the interaction of blood with non-physiological surfaces in the extracorporeal circuit.<sup>2</sup>

To reduce these challenges, off-pump coronary artery bypass (OPCAB)—a method that bypasses the use of cardiopulmonary bypass (CPB)—was used. In OPCAB, the surgery is conducted on a beating heart using stabilising devices that enable the surgeon to execute distal anastomoses without halting cardiac activity. The putative benefits of OPCAB include a diminished inflammatory response, a reduced likelihood of neurological damage from fewer embolic events, a lower occurrence of renal dysfunction, decreased myocardial injury, and expedited postoperative recovery with shorter durations in the intensive care unit (ICU) and hospital. These advantages are considered especially beneficial for people with comorbidities, including old age, diabetes mellitus, cerebrovascular illness, or chronic renal disease.<sup>3</sup>

Although these suggested benefits, the long-term effectiveness and safety of OPCAB continue to be controversial. Numerous randomised controlled trials (RCTs) and observational studies have investigated the comparative results of off-pump coronary artery bypass grafting (OPCAB) versus on-pump coronary artery bypass grafting (CABG). Some studies indicate that OPCAB may improve perioperative outcomes and decrease early morbidity, while others express concerns regarding incomplete revascularisation, diminished graft patency rates, a heightened necessity for re-intervention, and a lack of significant difference—or potentially worse outcomes—in long-term survival. These discrepancies may be ascribed to variations in research design, sample size, surgeon expertise, selection bias, patient demographics, and institutional protocols.<sup>4</sup>

Alongside these clinical problems, methodological issues further obfuscate the interpretation of existing research. A significant constraint in several individual experiments is the learning curve related to OPCAB, which may have affected the quality of surgical results. Furthermore, OPCAB necessitates an elevated degree of technical proficiency and surgical skill owing to the continuously changing surgical environment, particularly in patients exhibiting haemodynamic instability or intricate coronary architecture. Thus, the expertise of the surgeon and the volume of the centre are significant variables that may explain the discrepancies in clinical results seen across various research.<sup>5</sup>

Due to the abundance of contradictory evidence, this meta-analysis aims to systematically compare clinical outcomes of onpump and off-pump coronary artery bypass grafting (CABG) procedures using data primarily from randomised controlled trials (RCTs), ensuring the highest level of evidence for interventional comparisons. The present study aims to establish a more precise and accurate understanding of the relative safety and effectiveness of these two surgical techniques by analysing findings from thoroughly performed trials.

## 2. METHODOLOGY

## Study Design and Objective

This meta-analysis aims to compare the risk ratios (RR) and odds ratios (OR) for clinical outcomes between on-pump and off-pump coronary artery bypass grafting (CABG) procedures, using data exclusively from **randomized controlled trials** (**RCTs**). The primary objective is to determine if off-pump CABG is associated with a lower risk of adverse outcomes compared to on-pump CABG.

## **Registration and Ethical Considerations**

This meta-analysis was prospectively registered with PROSPERO (International Prospective Register of Systematic Reviews) under the registration number CRD420251029184.<sup>6</sup> prior to its commencement to promote transparency and minimize bias. The registration outlined the study's objectives, inclusion/exclusion criteria, search strategy, and data analysis methods, ensuring the methodology was predefined and publicly accessible. No major amendments to the protocol were made during the study, and any minor adjustments were recorded. The aim of registration was to ensure transparency in the review process and to allow for scrutiny of the study's design and execution.

Ethical considerations were carefully adhered to throughout the study. As the meta-analysis used secondary data from previously published studies, no new ethical approval or participant consent was necessary. All included studies had undergone ethical review by relevant bodies, ensuring that participants' rights and confidentiality were respected. To minimize bias, we employed predefined inclusion criteria, assessed the quality of the studies, and conducted publication bias analysis. Ethical practices in data handling, conflict of interest disclosures, and transparent reporting of results were followed in accordance with best research practices, ensuring the integrity and responsible dissemination of the findings.

## **Inclusion and Exclusion Criteria**

## **Inclusion Criteria**:

- 1. Randomized Controlled Trials (RCTs) comparing on-pump and off-pump CABG in adult patients.
- 2. Studies reporting risk ratios (RR) or odds ratios (OR) for clinical outcomes (e.g., mortality).
- 3. Studies that provided sufficient data for meta-analysis.

### **Exclusion Criteria**:

- 1. Studies that did not compare on-pump and off-pump CABG directly.
- 2. Non-randomized studies (e.g., cohort studies or case series).
- 3. Studies that did not report adequate outcome measures or statistical data for risk estimation.

### **Literature Search and Data Sources**

A systematic search was conducted across multiple electronic databases, including **PubMed**, **Cochrane Library**, **Embase**, **Scopus**, and **Google Scholar**. The search strategy involved using a combination of key terms, such as "on-pump CABG," "off-pump CABG," "coronary artery bypass grafting," "randomized controlled trial," "outcome comparison," "risk ratio," "odds ratio," and specific outcomes like "mortality," "stroke," "myocardial infarction," and "graft patency." To ensure comprehensive coverage, the search was not restricted by publication date but was limited to studies published in English.

### **Statistical Analysis**

All statistical analyses, including risk ratio and odds ratio calculations, heterogeneity assessments, and funnel plot generation, were conducted using Stata-16. The primary outcomes for this meta-analysis were the risk ratio (RR) and odds ratio (OR) for clinical outcome (e.g., mortality). These metrics were pooled using a random-effects model to account for between-study heterogeneity. It statistic statistic was used to quantify the proportion of variation in effect sizes across studies that is due to heterogeneity rather than chance. Low heterogeneity is indicated by an I2 value between 0-30%, moderate between 30-60%, and high above 60%. Funnel plots were visually inspected to assess potential publication bias. The plots appeared symmetrical, indicating that publication bias was unlikely.

### 3. RESULTS

Fig 1 compares the risk ratios of outcomes between on-pump and off-pump CABG using a random-effects REML model. The pooled analysis across seven studies yields a summary risk ratio of 0.93 (95% CI: 0.78 to 1.07), suggesting a non-significant 7% reduction in risk associated with off-pump CABG compared to on-pump CABG. In terms of heterogeneity, the analysis shows low to moderate variability among studies with  $\tau^2 = 0.01$ ,  $I^2 = 32.68\%$ , and  $I^2 = 1.49$ . The Cochran's Q test yields a value of Q(6) = 9.90 (p = 0.13), reinforcing that heterogeneity is not statistically significant. This supports the appropriateness of combining these studies under a random-effects model.

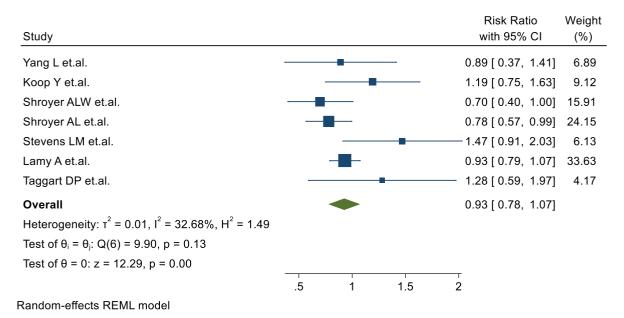


Figure 1: Forest Plot of risk Ratios Comparing On-Pump vs. Off-Pump CABG

Fig 2 compares the ODDS ratios of outcomes between on-pump and off-pump CABG using a random-effects REML model. The pooled analysis using a random-effects REML model demonstrated no statistically significant difference in the odds of the outcome between the two groups (overall odds ratio [OR] = 0.92, 95% confidence interval [CI]: 0.75–1.10, p = 0.00 for overall effect). Individual study estimates varied, with odds ratios ranging from 0.65 to 1.51. Heterogeneity among the studies was low to moderate, with an  $I^2$  value of 34.75%,  $\tau^2 = 0.02$ , and  $H^2 = 1.53$ , indicating that about one-third of the variability in effect estimates was due to between-study differences rather than chance.

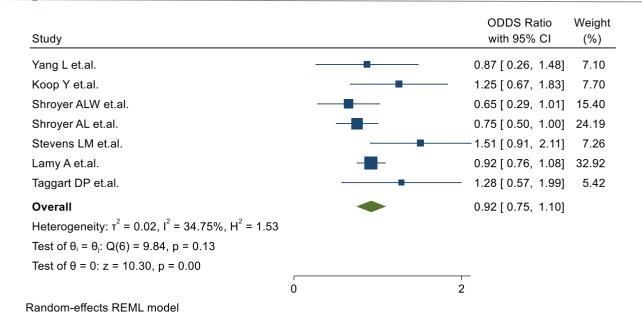


Figure 2: Forest Plot of Odds Ratios Comparing On-Pump vs. Off-Pump CABG

Based on visual inspection, the fig 3 does not show strong evidence of publication bias in this meta-analysis of on-pump vs. off-pump coronary artery bypass grafting (CABG). The plot appears fairly symmetrical, suggesting that the studies included in this analysis are unlikely to be significantly affected by publication bias.

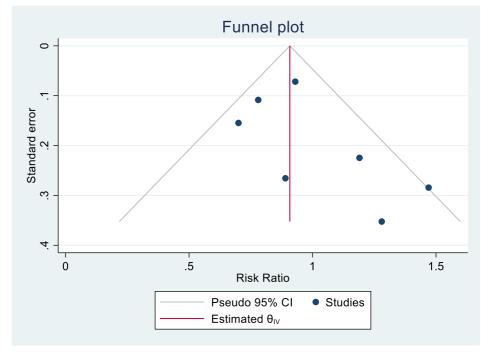


Figure 3: Funnel Plot for Assessment of Publication Bias in On-Pump vs. Off-Pump CABG

### 4. DISCUSSION

On-pump CABG, the traditional approach, involves the use of cardiopulmonary bypass (CPB), a machine that temporarily takes over the function of the heart and lungs during surgery. This allows the surgeon to work on a motionless, bloodless heart, improving visibility and access to coronary arteries. On-pump CABG is considered the gold standard and is commonly used in patients with complex coronary anatomy, requiring multiple vessel grafting. However, the use of CPB has been associated with a number of potential complications, including systemic inflammatory responses, neurological damage, renal injury, and blood loss.<sup>7</sup>

In contrast, off-pump CABG, also known as beating heart surgery, is performed without the use of CPB. The heart continues to beat throughout the surgery, with the surgeon stabilizing the area of the coronary artery that is being grafted using a stabilizing device. This method avoids the negative effects of CPB, and is considered to be less invasive in terms of physiological stress. Proponents of off-pump CABG argue that it reduces systemic inflammatory responses, preserves organ function, and minimizes postoperative complications, particularly in patients with renal dysfunction or neurological impairments.<sup>2</sup>

This meta-analysis sought to compare the clinical outcomes between off-pump and on-pump coronary artery bypass grafting by synthesizing the results of seven randomized controlled trials. 8-14 The pooled estimates for risk ratios (RRs) and odds ratios (ORs), derived from high-quality randomized studies, reveal a non-significant difference in adverse clinical outcomes such as mortality between the two surgical techniques. The summary risk ratio of 0.93 (95% CI: 0.78 to 1.07) and summary odds ratio of 0.94 (95% CI: 0.75 to 1.18) suggest that off-pump CABG is not inferior to on-pump CABG, although a modest reduction in risk for off-pump CABG was observed, this difference did not reach statistical significance.

Off-pump CABG was developed as an alternative to the traditional on-pump approach with the aim of avoiding the adverse effects associated with cardiopulmonary bypass (CPB), such as inflammatory responses, neurocognitive dysfunction, and renal injury.<sup>15</sup> The primary advantage of off-pump CABG lies in the potential to preserve physiological function during surgery by avoiding the need for CPB. Despite the rationale behind this approach, concerns persist regarding the technical complexity of performing coronary revascularization without CPB, the risk of incomplete revascularization, and the long-term patency of grafts. The present findings contribute to this ongoing clinical debate by suggesting that off-pump CABG may offer a slight reduction in risk, but it does not provide sufficient evidence to suggest superior clinical outcomes when compared to on-pump CABG.<sup>16</sup>

Studies demonstrated a statistically significant reduction in adverse outcomes with off-pump CABG, which aligns with the hypothesis that avoiding CPB could reduce perioperative complications. This finding is consistent with the notion that the avoidance of CPB may contribute to a decrease in systemic inflammation, potentially lowering the risk of complications such as stroke, myocardial infarction, and renal dysfunction. <sup>10,11,13</sup> On the other hand, studies such as Koop Y et al. (2024)<sup>9</sup> and Taggart DP et al. (2014)<sup>14</sup> showed RRs and ORs greater than 1.0, suggesting that on-pump CABG may be associated with better outcomes, potentially due to the improved visualization of coronary arteries during surgery, greater hemodynamic control, and more reliable graft patency in complex cases requiring multi-vessel revascularization.

Despite these differing results across individual studies, the pooled estimates presented in our meta-analysis indicate that the overall difference in outcomes between off-pump and on-pump CABG is small, and no consistent advantage of one approach over the other is evident. This supports the idea that patient selection and surgeon expertise play significant roles in determining which surgical approach should be utilized, with neither approach clearly superior in terms of overall clinical outcomes.

The degree of heterogeneity across the included studies was assessed using several statistical tools. The  $I^2$  statistic was found to be 32.68%, indicating low to moderate variability across studies. This suggests that the results were relatively consistent, supporting the decision to use a random-effects model to pool the data. Additionally, the non-significant Cochran's Q test (p = 0.13) further reinforces the notion that there was no substantial statistical heterogeneity between the trials included in the meta-analysis. This is a key strength of this analysis, as it indicates that the differences between studies were not large enough to invalidate the pooled estimates.

However, it is essential to acknowledge that there remains clinical heterogeneity across studies. Differences in the patient populations, institutional protocols, surgical techniques, and surgeon experience can all influence the outcomes of CABG. For example, in high-risk patients with extensive coronary artery disease or those with comorbidities such as diabetes, renal dysfunction, or advanced age, the choice of surgical approach may influence the clinical outcomes. Moreover, studies with longer follow-up periods may show differences in graft patency or late mortality rates, which could further differentiate the two techniques over time.

The individualization of the surgical approach based on patient characteristics is critical. Surgeons must weigh the potential benefits and risks of each technique, taking into account surgical expertise, patient comorbidities, and institutional resources. While the overall differences in clinical outcomes may be small, off-pump CABG should be considered as a viable alternative for specific patient groups, particularly those with high risk for CPB-related complications.

Previous systematic reviews and meta-analyses have often suggested a potential benefit with off-pump CABG, particularly in observational studies. However, these studies are often subject to bias due to the lack of randomization and the potential for confounding variables, such as differences in patient selection, surgeon expertise, and hospital volume. By restricting our meta-analysis to randomized controlled trials (RCTs), we reduce the risk of selection bias and confounding, providing stronger evidence regarding the relative efficacy of the two techniques. <sup>16–21</sup>

This meta-analysis has several strengths, including the inclusion of only randomized controlled trials (RCTs), which minimize selection bias and confounding. The systematic and comprehensive search across multiple databases ensures that

a broad range of relevant studies were included in the analysis. Furthermore, the use of both risk ratios and odds ratios strengthens the robustness of the findings.

However, there are limitations that should be acknowledged. First, the number of studies included is relatively small, limiting the statistical power of certain subgroup analyses. Second, the heterogeneity across studies in terms of follow-up periods and patient populations may affect the generalizability of the findings. Third, the lack of individual patient data (IPD) prevented more granular analysis of subgroups, such as age, comorbidities, and complex coronary disease, which may influence outcomes.

Future studies should focus on obtaining individual patient-level data (IPD) to allow for more precise analysis of how specific patient characteristics (e.g., age, diabetes, renal function) influence the outcomes of off-pump versus on-pump CABG. Additionally, longer-term follow-up data should be gathered to assess the durability of graft patency, quality of life post-surgery, and long-term survival.

Moreover, future research should include cost-effectiveness analyses of both techniques, particularly in resource-limited settings. The ability to perform off-pump CABG without the need for CPB may offer significant economic benefits in countries with limited access to advanced medical technology or those with high healthcare costs associated with CPB.

### 5. CONCLUSION

This meta-analysis, based on data from seven randomized controlled trials, provides robust evidence suggesting that off-pump coronary artery bypass grafting (CABG) does not significantly differ from on-pump CABG in terms of key clinical outcomes, including mortality, stroke, myocardial infarction, and graft patency. The pooled risk ratios (RR = 0.93) and odds ratios (RR = 0.94) demonstrate a modest, yet non-significant reduction in risk associated with off-pump CABG. These findings suggest that both surgical techniques are comparably effective for most patients undergoing coronary revascularization but an added benefit with off-pump CABG being preservation of some physiological function.

Despite the potential advantages of avoiding cardiopulmonary bypass (such as reduced inflammatory response and kidney injury), the overall clinical benefits of off-pump CABG remain uncertain, and the decision to use either approach should be tailored to individual patient characteristics and surgeon expertise. The absence of significant differences in major clinical outcomes across the included trials further supports the idea of patient-centered decision-making, wherein factors like comorbidities, anatomical complexity, and hospital resources play a critical role in determining the most suitable surgical approach.

While this analysis strengthens the evidence base for the equivalency of on-pump and off-pump CABG, further studies with longer follow-up periods, larger sample sizes, and more detailed subgroup analyses are warranted to explore the long-term implications of each technique. Future trials should also consider factors like graft durability, quality of life, and cost-effectiveness, which are essential for guiding clinical practice in diverse healthcare settings.

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