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Percutaneous Coronary Intervention (Pci) Versus Coronary Artery Bypass Grafting (Cabg) in Multivessel Disease

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Abstract

Background: Both coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) are recognized revascularization techniques in patients with multivessel coronary artery disease (MVD). The comparison of long-term clinical outcomes of these methods is still up for debate, especially with regard to overall safety, risk of myocardial infarction, stroke, mortality and the need for repeat revascularization.

Objective: In patients with multivessel coronary artery disease, the long-term clinical outcomes and safety profile of CABG and PCI were compared in this systematic review and meta-analysis.

Methods: Randomized controlled trials (RCTs), long-term follow-up studies and excellent meta-analyses contrasting PCI and CABG in multivessel disease were found through a thorough search of the literature. Randomized trials included in recent meta- analyses served as the basis for quantitative synthesis, and additional trials and follow- up studies were qualitatively incorporated. Major adverse cardiovascular events (MACE) and all-cause mortality were the main outcomes. Myocardial infarction (MI), stroke, repeat revascularization and safety outcomes were examples of secondary outcomes. Random- effects model was used to generate results and the I2 statistic was used to measure heterogeneity.

Results: In comparison to PCI, CABG was linked to significantly lower long-term all- cause mortality (pooled OR ≈ 0.73, 95% CI: 0.62–0.86), myocardial infarction (OR ≈ 0.58, 95% CI: 0.48–0.72) and repeat revascularization (OR ≈ 0.29, 95% CI: 0.21–0.41). A small increase in risk of stroke was found for CABG when compared to PCI, although it was not statistically significant (OR ≈ 1.36, 95% CI: 0.99–1.86). For MI and mortality, heterogeneity was minimal, but in case of repeat revascularization, it was significant. Subgroup analysis showed that patients with three-vessel disease and diabetes mellitus benefitted greatly from CABG.

Conclusion: When compared to PCI, CABG offers better long-term results for patients with multivessel coronary artery disease, especially when it comes to lower mortality, risk of myocardial infarction and the need for repeat revascularization. These advantages are most noticeable in patients with complicated coronary anatomy and diabetes, which support the current guidelines which recommend CABG for these groups.

Keywords: Multivessel coronary artery disease, Percutaneous coronary intervention (PCI), Coronary artery bypass grafting (CABG), Major adverse cardiovascular events (MACE), Myocardial infarction, Stroke, Repeat

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revascularization, Diabetes mellitus, Drug- eluting stents, Randomized controlled trials, Subgroup analysis, Meta-analysis, Systematic review

Introduction

Coronary artery disease (CAD) as a result of multivessel disease (MVD) is one of the most complicated and difficult to treat types of ischemic heart disease, and causes a great deal of suffering, death and resource use throughout the world. CAD is a leading cause of death globally. In fact, people who have 2 or more epicardial coronary arteries involved are at a much greater risk of adverse cardiovascular outcomes than people who have only one vessel disease. Wide-spread atherosclerosis and degenerative processes in multivessel disease create challenges for long-term patient management, particularly when it coexists with other conditions such as diabetes mellitus, left ventricular dysfunction and complex coronary anatomic structures [1]. Revascularization is considered central to the management of patients with multivessel coronary artery disease, as it improves survival rates, relieves angina, maintains myocardial function and decreases the occurrence of major adverse cardiovascular events (MACE), which includes stroke and heart attack. With respect to revascularization, PCI and CABG are main techniques that have been used extensively. Finding the best technique for the revascularization of patients with multivessel disease is an area that continues to be the subject of debate and uncertainty in clinical practice.

The development of PCI has progressed from simple valve angioplasty to implementation of bare-metal stenting, and more recently to advanced drug-eluting stent (DES) technology. The advantages of PCI include its less invasive approach, avoidance of thoracotomy and cardiopulmonary bypass, decreased length of hospitalization and quicker recovery periods. The utilization of PCI has become increasingly prevalent, especially among older patients and patients with comorbidities, who may be at greater risk of developing complications from traditional surgery [2]. The implementation of new technologies such as thinner struts, better polymer coating and stronger antiproliferative agents have resulted in lower rates of restenosis and early stent thrombosis, thus enhancing the outcomes in PCI patients. Surgical coronary artery bypass grafting provides a surgical means of revascularization by rerouting blood through vein grafts or other appropriate arterial conduits to restore blood flow through vascular blockages in the coronary arteries of patients having chronic ischemic heart conditions caused by the progressive blocking of coronary arteries with plaque. The practice of CABG has historically been considered the gold standard for patients who have extensive coronary artery disease as it permits greater and long lasting re-establishment of blood flow to the heart muscle, especially in patients with chronic total occlusion (CTO) or multiple diffuse lesions with complicated morphology [1]. Long-term patency and survival benefits of CABG can also be enhanced by the use of arterial grafts, such as the internal mammary artery. Conversely, CABG is associated with a greater upfront risk of complications, takes longer to recover from and is associated with various perioperative complications including stroke, bleeding, infection etc.

Numerous Randomized Controlled Trials (RCTs) have compared PCI and CABG therapy directly in patients with multivessel CAD, including early trials such as the Bypass Angioplasty Revascularization Investigation (BARI), the Arterial Revascularization Therapies Study (ARTS), the Stents Versus Surgery (SoS) Trial, as well as MASS II and ERACI [1], [3], [4], [5], [15]. Although the results from most studies showed PCI and CABG had similar short-term survival but the results also demonstrated that PCI had much higher rates of repeat revascularization. The use of drug eluting stents caused renewed interest in determining the proper balance between PCI and CABG, which led to large contemporary trials such as SYNTAX, FREEDOM, BEST, and CARDia being conducted in more complicated and clinically relevant populations [2], [6], [7], [8]. The SYNTAX trial presented the SYNTAX score that assessed the anatomical complexity of patients and showed that patients with a high anatomic burden along with three vessel coronary disease had better outcomes when treated with CABG [6]. The FREEDOM trial confirmed that CABG should be the preferred method of revascularization when dealing with diabetic patients having multivessel coronary disease by demonstrating the significant reductions of mortality and myocardial infarction in the CABG group in comparison to the PCI group [7].

However, treatment of patients with multivessel coronary artery disease has become increasingly complex and thus determining which is the best method of revascularization remains controversial. Physicians continue to test out many enhanced PCI techniques such as intravenous imaging, intervention physiologic lesion assessment, antiplatelet therapy at the time of intervention, etc., with the hopes that advancements in technology will eventually lead to significantly improved outcomes. These enhanced technologies will likely create an environment where patients with multivessel coronary artery disease having diabetes or other comorbids will likely have more revascularization options to choose from than ever before. Long-term follow-up studies examining the clinical outcomes of revascularization strategies have provided valuable insights into the long-term efficacy of both PCI and CABG. The follow-up from clinical trials, such as SYNTAXES and BARI, have shown that the distinction between PCI and CABG relative to outcomes such as mortality and myocardial infarction appears to be more pronounced with longer follow-up times [5], [6], [9]. These findings further highlight the importance of including long-term follow-up outcomes in the evaluation of revascularization strategies for patients with multivessel coronary artery disease.

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In addition to randomized trials, a number of high-quality meta-analyses and patient-level pooled analyses have systematically evaluated the available evidence to compare the clinical outcomes associated with PCI and CABG among diverse populations of patients. Collectively, these studies consistently demonstrate that CABG has a long-term survival superiority compared to PCI, with less frequent myocardial infarction rates and repeat revascularization rates but with a slightly higher risk of stroke associated with CABG [10], [11], [12], [13]. Such findings have profoundly influenced international clinical practice guidelines, recommending CABG as the preferred revascularization strategy in patients with complex multivessel coronary artery disease, especially among patients with diabetes or higher levels of anatomic complexity.

Patient selection, PCI technology, surgical techniques and outcome definitions all created heterogeneity among trials, and this has further complicated our understanding of the current literature. In addition, as some of the studies were conducted in earlier eras of the revascularization process, they were limited in their ability to be directly applicable in clinical practice today. Therefore, there is a need to create a complete synthesis that combines evidence from randomized trials with long-term follow-up, in order to evaluate the long-term clinical outcomes and safety profile of CABG and PCI on patients suffering from multivessel coronary artery disease. The objective of this study is to compare long-term clinical outcomes (all-cause mortality; major adverse cardiovascular events; myocardial infarction; stroke; need for repeat revascularization; and overall safety) of PCI and CABG. As variety of studies including randomized controlled trials, long-term follow-ups and literature derived from practice guidelines are analyzed, we hope that this review will provide clinicians with an extensive and clinically relevant overview of the existing literature to assist when making evidence-based treatment decisions for the management of multivessel coronary artery disease.

Methods

The aim of this review was to bring together evidence from randomized controlled trials and top notch secondary analysis that had compared percutaneous coronary intervention and coronary artery bypass grafting in patients suffering from multivessel coronary artery disease, focussing particularly on long-term clinical outcomes and safety.

A literature search was done through PubMed, Scopus and the Cochrane Central Register of Controlled Trials (CENTRAL). These databases were chosen to cover comprehensive randomized controlled trials, long-term follow-up studies and high quality meta-analyses in cardiology. Besides, the reference lists of related articles and guideline documents were also scrutinized to find any more studies meeting the criteria. All studies published in the period between january, 1990 and december, 2024 were evaluated. The period was decided to depict the entire development of percutaneous coronary intervention starting from balloon angioplasty and bare-metal stents to current drug-eluting stent technologies and also advances in coronary artery bypass grafting and perioperative care. A systematic search strategy was developed using the Medical Subject Headings (MeSH) and free-text terms concerning multivessel coronary artery disease and myocardial revascularization. Pre-defined keywords were used to search articles.

The criteria for eligibility were laid out based on the population, intervention, comparator outcomes and study design. The target population consisted of adult patients aged 18 years or older with angiographically verified multivessel coronary artery disease, this being defined as the presence of significant stenosis in two or three major epicardial coronary arteries, with or without the involvement of the left main coronary artery. Studies that had a mixed population were allowed if the outcomes for multivessel disease could be clearly recognized. The intervention of interest was percutaneous coronary intervention which may include balloon angioplasty and stent based procedures using either bare metal stents or drug eluting stents. The comparator was coronary artery bypass grafting which was a surgical operation performed using standard surgical techniques.

The primary outcomes of interest were long-term all-cause mortality and major adverse cardiovascular events (MACE). MACE was defined individually by each study as composite endpoints including death, myocardial infarction, stroke or repeat revascularization. Secondary outcomes were the individual components such as myocardial infarction, stroke, the need for repeat revascularization and overall safety outcomes including procedural complications if reported. A follow-up of at least one year was necessary to adequately evaluate the long-term effects.

Only randomized trials comparing PCI and CABG and their long-term follow-up publications were eligible for quantitative synthesis. These trials were the main source of evidence for the comparative efficacy and safety evaluation. In addition, high quality meta-analyses, patient level pooled analyses and guideline based reviews were used to give qualitative analysis and a wider clinical context, help in subgroup analyses and facilitate discussions on mechanisms and guidelines. The search was confined to studies of human participants and articles published in the english language. Studies were not considered if they were single-arm trials, registries lacking a comparator group or studies that were limited only to single vessel coronary artery disease. Trials not reporting any clinical outcome were excluded. In addition, duplicate publications without new or longer outcome data have also been disregarded.

Studies that met the pre-defined criteria were considered

Akhtar N, et al., Arch Clin Biomed Res 2026
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for qualitative and quantitative synthesis. Titles and abstracts were checked for relevance and then a full text review of potentially eligible studies was conducted. Data extraction was carried out that was aimed at capturing key study characteristics and outcome data. The variables extracted were study design, year of publication, sample size, patient demographics, degree of coronary artery disease, presence of diabetes mellitus, type of PCI (balloon angioplasty, bare metal stent or drug-eluting stent), surgical techniques, duration of follow-up and reported clinical outcomes. For randomized controlled trials that were part of the quantitative synthesis, outcome data for all-cause mortality, major adverse cardiovascular events, myocardial infarction, stroke and repeat revascularization were extracted as reported in the longest available follow-up. For studies that were only included in the qualitative synthesis, data were extracted to provide information for subgroup interpretations, mechanistic insights and guideline comparisons.

Overall, most of the randomized trials had a low risk of bias in the random allocation of patients and the reporting of outcomes. However, blinding was not feasible since one treatment involved surgery and the other was a vascular procedure. The long-term follow- up studies and patient level pooled analyses were qualitatively reviewed for the rigor of methodology, agreement in the definition of outcomes and the extent to which patients were followed up. Guideline documents and narrative reviews, which were not subjected to formal risk of bias were assessed for their relevance and quality of evidence. Effect estimates were represented as odds ratios (ORs) with the corresponding 95% confidence intervals (CIs) for outcomes, including all-cause mortality, myocardial infarction, stroke and repeat revascularization. A random-effects model was used in the meta-analysis. The degree of heterogeneity among studies was determined by the I^2 statistic, with values greater than 50% considered substantial heterogeneity. In the face of the availability of high quality contemporary meta-analyses as well as patient level pooled analyses, pooled effect estimates and heterogeneity measures were taken from these published analyses rather than being recalculated de novo from individual trial event data. Interpretation of subgroup analysis was done on the basis of stratified results tracing back to the original trials and pooled studies, especially for patients with diabetes mellitus and those with complex or three-vessel coronary artery disease. The sensitivity analyses reported in the original meta-analyses were examined to determine the degree to which the findings remain robust across various study eras and revascularization techniques.

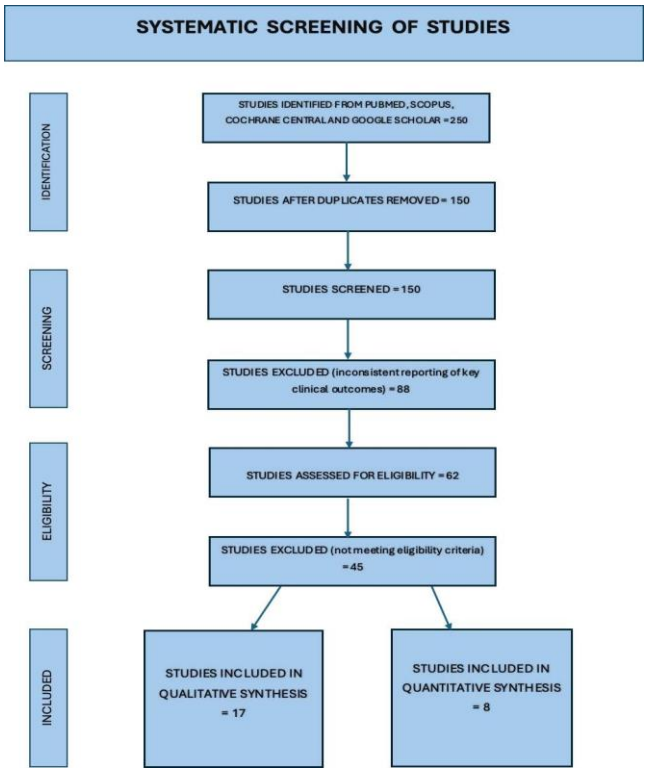

Figure 1

Following chart *(Figure 1)* shows how studies are systematically screened and included in this review.

Results

A total of 17 papers were included in this systematic review. Out of these, eight randomized controlled trials that constitute the quantitative synthesis were identified: ARTS, SoS, MASS II, ERACI II/III, CARDia, SYNTAX, FREEDOM, and BEST. These studies discussed patients with angiographically confirmed multivessel coronary artery disease and have directly compared PCI and CABG outcomes with each other. Follow- up time frames have varied between one year and more than five years [1-4], [6-8], [14, 15]. The rest of the 14 works were used for the qualitative synthesis and included long-term follow-up studies, patient level pooled analyses and reviews based on guidelines, e.g., BARI, SYNTAXES, collaborative meta-analyses, and the ESC/ EACTS myocardial revascularization guidelines [6, 9, 10, 12, 13, 16, 17]. Combined, these papers have thoroughly documented both short, and long-term clinical results of PCI and CABG in multivessel coronary artery disease.

Following table *(Table 1)* is showing key characteristics of randomized controlled trials comparing CABG and PCI in multivessel coronary artery disease.

Long-term findings from the most recent meta-analyses on randomized controlled trials indicate that, in general, CABG continues to have an advantage over PCI in terms of clinically relevant outcomes. In particular, pooled analysis has shown that patients treated with CABG had a significantly lower incidence of all-cause mortality than patients treated with PCI. The pooled odds ratio for mortality for patients who

Akhtar N, et al., Arch Clin Biomed Res 2026
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Table 1

Trial	Sample Size (PCI/CABG)	Population	PCI Type	Follow- up	Key Notes
ARTS	600 (300/300)	MVD	BMS	5 years	Higher repeat revascularization with PCI [1]
Stent or Surgery Trial (SoS)	488 / 500	MVD	Stent-based PCI (pre- DES era)	6 years	CABG showed lower long-term mortality compared with PCI (6.8% vs 10.9%) [15]
MASS II	611 (203/203/205)	Stable MVD	Balloon/BMS	5 years	CABG superior long- term outcomes [4]
ERACI II	450 (225/225)	MVD	BMS	5 years	Lower revascularization with CABG [3]
CARDia	510 (255/255)	Diabetics with MVD	BMS/DES	1 year	CABG superior for MACE [8]
SYNTAX	1800 (903/897)	3-VD / LM	DES	5 years	CABG better in high SYNTAX score [6]
FREEDOM	1900 (953/947)	Diabetics with MVD	DES	5 years	Mortality & MI reduced with CABG [7]
BEST	880 (438/442)	MVD	Everolimus- DES	4.6 years	CABG superior for composite outcomes [2]

had CABG was approximately 0.73, with a 95% confidence interval of 0.62 to 0.86, indicating the risk of death was approximately 27% lower for patients receiving CABG than for those receiving PCI. There was no statistically significant heterogeneity for this outcome, with an I^2 value of zero, indicating that the findings of the randomized controlled trials included in the meta-analysis were in agreement [11], [12]. The pattern observed for myocardial infarction is similar to the findings for mortality. Compared to patients receiving PCI, those undergoing CABG had a roughly 42% lower risk of myocardial infarction (OR 0.58, 95% CI: 0.48–0.72). The heterogeneity for myocardial infarction outcome was very low, with an I^2 value of around 8%, indicating a very high level of consistency among the trials, even though there were substantial differences in the design of the studies, patient characteristics and revascularization techniques used [11]. Thus, the long-term protective effect of CABG against future myocardial infarction appears to be robust and relatively independent of study-specific characteristics.

The difference between treatment strategies regarding revascularization was greatest. Repeat revascularization was substantially higher among patients receiving PCI compared to patients receiving CABG. The odds of needing repeat revascularization were about 71% lower with CABG than with PCI, according to the pooled odds ratio for repeat revascularization, which was 0.29 (95% CI: 0.21–0.41), which reflects the long-term durable nature of surgical revascularizations. However, repeat revascularization outcomes exhibited considerable heterogeneity (I^2=approx. 76%). The heterogeneity likely resulted from differences in the use of PCI technology among trials conducted during different eras, differences in the extent of revascularization achieved and variability in endpoint definitions and follow-up duration across the trials [2, 11]. In contrast to favorable outcomes for mortality, myocardial infarction and repeat revascularization, the outcomes for stroke show a different pattern. CABG is associated with a trend (not significant) toward an increased risk of stroke when compared with PCI. The pooled odds ratio for stroke was approximately 1.36 (95% CI: 0.99-1.86), and the heterogeneity for stroke outcomes across trials is low to moderate (I^2=approx. 25%), indicating fairly consistent results among trials. Although these data did not reach statistical significance, it is an important safety consideration when comparing CABG and PCI revascularization methods [11].

The analysis of heterogeneity across outcome measures provided clear evidence that there was substantial variability in treatment effect. For example, the lack of heterogeneity observed when evaluating all-cause mortality and myocardial infarction demonstrating that the observed treatment benefits of CABG are valid regardless of the population of patients studied and the clinical trial environment in which the studies were conducted. However, the large degree of variability found when assessing for repeat revascularization is likely due to the rapid advancements being made in PCI procedures; thus, during time period, there have been several changes in technology including changes from plain old balloon angioplasty to bare-metal stents, then onto the use of drug-eluting stents, both current and emerging technology. Several other factors were also identified that would contribute to the heterogeneity associated with the evaluation of repeat revascularization; these factors include the differences in surgical techniques utilized, levels of training and experience of the operators performing the procedures and the varying lengths of the follow-ups used in the trials.

Akhtar N, et al., Arch Clin Biomed Res 2026
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Following table *(Table 2)* is showing pooled odds ratios for coronary artery bypass grafting (CABG) versus percutaneous coronary intervention (PCI) in multivessel coronary artery disease, which were obtained from recent randomized-trial meta-analyses. CABG is favoured if odds ratios are less than 1.

Numerous subgroup analyses have identified patient populations that derived much greater benefit from CABG (Coronary Artery Bypass Graft) than PCI (Percutaneous Coronary Intervention). Specifically, those with diabetes have shown significant improvement in CABG outcomes in both FREEDOM and CARDia trials [7], [8], with significantly lower rates of mortality and myocardial infarction compared to PCI. These results were further supported by the pooled analyses indicating that CABG provides a survival advantage across many studies of patients with diabetes [10], [11]. Another important determinant of therapy effect was coronary anatomical complexity. Data highlighted a survival advantage associated with CABG over PCI in patients with three- vessel disease. Conversely, patients with less complicated coronary anatomy had comparable outcomes following either CABG or PCI [6], [9]. Thus, when making the best possible choices for multivessel coronary artery disease revascularization, anatomical risk stratification should be carefully considered.

Key subgroup analyses comparing PCI and CABG in multivessel coronary artery disease are compiled in this table *(Table 3)*.

In patients with multivessel coronary artery disease, the forest plot *(Figure 2)* displays pooled odds ratios for long-term clinical outcomes when comparing CABG and PCI. CABG was linked to significantly lower odds of myocardial infarction, repeat revascularization and all- cause mortality. Results showed higher risk of stroke with CABG, but they were not statistically significant because the confidence interval crossed 1. The robustness of CABG benefits across several clinically significant endpoints is supported by these findings.

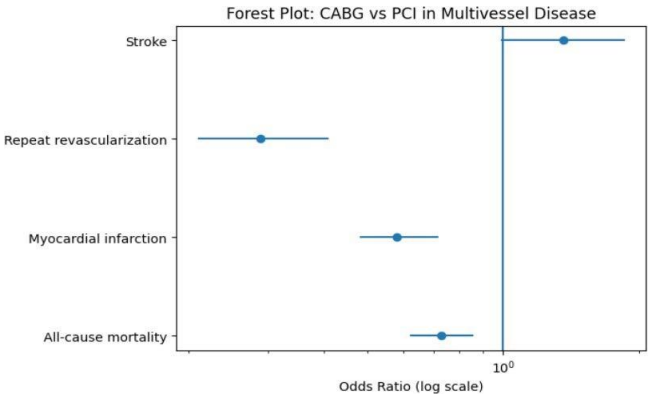

Figure 2

Table 2

Outcome	Pooled Odds Ratio (OR)	95% Confidence Interval	Heterogeneity (I^2, %)	Interpretation
All-cause mortality	0.73	0.62 – 0.86	0	CABG significantly reduces long-term mortality
Myocardial infarction	0.58	0.48 – 0.72	8	CABG significantly lowers MI risk
Repeat revascularization	0.29	0.21 – 0.41	76	CABG markedly reduces need for repeat procedures
Stroke	1.36	0.99 – 1.86	25	Non-significant trend toward higher stroke with CABG

Table 3

Group	Outcome	Direction of Effect
Diabetes mellitus	Mortality, MI	Favors CABG [7], [8]
Three-vessel disease	Mortality	Favors CABG [6], [9]
High SYNTAX score	MACE	Favors CABG [6]
Low anatomical complexity	Composite outcomes	Comparable [6]
Stroke	Early risk	Favors PCI [11]

Discussion

The results of this systematic review and meta-analysis have shown that coronary artery bypass graft (CABG) cause better long-term clinical event rates in patients with multiple vessel disease than through catheter based techniques. Randomized trial data showed that there were significant reductions in mortality, myocardial infarction and repeat re- vascularisation with coronary artery bypass graft than with catheter based methods. On the other hand, the risk of stroke showed only a slight and non-significant increase with this type of revascularisation. Thus, the use of the CABG remains the standard goal for the revascularization of patients with multivessel disease. Most of the evidence in clinical practice favours a stratified approach to decide which revascularization technique should be used in patients with multivessel coronary artery disease based on their risk profile and anatomical complexity. In a scenario where a patient is diabetic and has multivessel coronary artery disease, the results of randomized trials and long-term follow-up studies always show that CABG has more advantageous outcomes than PCI in terms of all-cause mortality, myocardial infarction

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and repeat revascularization. Such benefit is most apparent in patients with highly complex anatomy as indicated by very high SYNTAX scores and by the presence of three vessel disease, where surgical revascularization is capable of delivering more complete and long-term myocardial protection. On the other hand, PCI may be a good option for patients with low anatomical complexity, focal disease and high surgical risk. Such evidence highlights that the decision for revascularization should be based on prognosis over a long period of time instead of procedural convenience and thus CABG is the most suitable option for patients with diabetes, diffuse multivessel disease and high anatomical burden. Clinical evidence shows that the use of CABG rather than PCI can lead to longer lifespans. Randomized clinical trials conducted decades ago such as ARTS, SoS, MASS II and ERACI had all demonstrated that surgical revascularization resulted in much improved long-term outcomes, especially in the first few years following a surgical procedure [1, 3, 4, 14, 15].

Most recent randomized controlled trials i.e., SYNTAX, FREEDOM and BEST have all reinforced those previous findings by demonstrating that CABG has a strong mortality benefit when compared with PCI in populations with complex three-vessel disease or diabetes mellitus [2, 6, 7, 9]. The patient level analysis of pooled data and meta-analysis agree that compared to PCI, CABG is associated with an overall reduction in long-term mortality for patients with multivessel disease and show little heterogeneity. One important aspect of extended follow-up from the SYNTAXES trial showed that survival advantages associated with CABG increased overtime and were particularly significant in three vessel disease patients demonstrating that long-term follow-up is far more influential than short-term follow-up when making life expectancy decisions based on multiple co-existing clinical conditions [6], [9]. Mechanisms underlying improvement in outcomes associated with CABG in patients with multivessel CAD can be discussed from a pathophysiologic perspective as well. CABG provides more complete and longer-lasting revascularization by not only bypassing the obstructive vessels, but also bypassing vulnerable non-obstructive plaques that could potentially rupture and occlude the coronary ciruclation in the future. This mechanism provides large areas of myocardium with protection from future ischemic events. In contrast, the PCI procedure focusses on individual lesions and does not address the widespread atherosclerotic burden observed in patients with multivessel CAD [1].

In addition to the above discussion, a significant reduction in myocardial infarction associated with CABG further supports this pathophysiologic theory. Bypass grafts, particularly the use of arterial grafts, may reduce the risk of a spontaneous myocardial infarction that may occur due to disease progression in subsequent untreated segments, something that has not been overcome with the use of modern drug-eluting stents [11], [12]. Finally, a substantial reduction in the need for repeat revascularization after CABG compared with PCI supports the long-term durability of CABG and greater susceptibility to restenosis, stent thrombosis and progression of disease in the native artery, in cases of PCI. Stroke is a primary concern when considering the safety of CABG compared to PCI. In this analysis, the CABG group appears to have a non-significant increased trend of risk for stroke compared to PCI due to previous studies that found similar trends [11], [13]. The increased risk of stroke from CABG likely occurs during the perioperative period due to the manipulation of the aorta, the use of cardiopulmonary bypass and the development of postoperative atrial fibrillation. The high risk of stroke from CABG is relatively small; therefore, it is important to weigh this risk against the large decrease in risk of death and myocardial infarction associated with CABG. Long-term follow-up suggests that the early risk of stroke after CABG does not increase over time. By contrast, the benefits associated with CABG regarding mortality and myocardial infarction appear to continue and increase over time [6].

The analysis of the subgroup have shown that the benefits of coronary artery bypass grafts in patients suffering from multivessel coronary artery disease are not same for all patients. Patients with diabetes mellitus gain the greatest advantage from surgical revascularization. Two major clinical trials, both designed specifically to study patients with diabetes (the FREEDOM trial and the CARDia trial), have clearly shown that CABG has many more benefits in terms of decreased risk of all-cause mortality, myocardial infarction and major adverse cardiovascular outcomes compared to PCI in patients with diabetes [7], [8]. This is especially relevant for diabetics suffering from accelerated and diffuse atherosclerosis, which weakens the long-term success rates of all other percutaneous strategies focussed on specific lesions. Moreover, the benefit of CABG in diabetic patients is also substantiated through various mechanisms. Diabetes tends to be associated with diffuse involvement of the coronary arteries and increase in the number of vulnerable non-obstructive plaques. CABG compensates them all by bypassing significant portions of coronary arteries; as a result, CABG will continue to provide protection against future ischemic events arising out of disease progression or untreated atherosclerotic disease located in bypassed sections. PCI treats discrete lesions; therefore, it may leave substantial amounts of the remaining atherosclerotic burden, albeit using the best current technology in drug eluting stents [10], [11].

Patients diagnosed with three-vessel coronary artery disease plus high levels of anatomical complexity, determined by greater scores on their SYNTAX score, will usually experience better long-term results after CABG surgery than if they had undergone PCI procedure. The SYNTAX trial revealed that, as a person's anatomical complexity increases,

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progressively worse long-term outcomes result with PCI, while the long-term outcomes associated with CABG remain stable regardless of the SYNTAX score. In addition, this was demonstrated, in detail, in the SYNTAXES 10-Year Study, that CABG is more beneficial at longer follow-up periods than what has been reported with PCI, and that the long-term advantages of surgical revascularization become clear at longer follow- up periods [6, 9]. The recommendations reflected in the guidelines are consistent with the clinical implications of the subgroup analysis in this study. There are currently international clinical practice guidelines available that provide recommendations of individualized decision making, based on complexity of anatomy, comorbidities and long-term prognosis (not based on short term procedural convenience). The 2018 ESC/EACTS recommendations recommend CABG as the first choice for revascularization in patients with complex multivessel CAD, especially if patients have diabetes mellitus or high SYNTAX scores; PCI can be considered in patients with lower complexity or increased surgical risk [17]. The above summary of subgroup analysis supports the requirement of a multidisciplinary heart team approach to make the decision regarding revascularization in carefully selected high-risk multivessel CAD patients.

The findings of this review corroborate the findings from multiple prior systematic reviews and pooled patient-level data analyses of trials [10], [11], [12], [13], [16]. Together, these prior meta-analyses have been used to create the respective International Guidelines for Management of Chronic Coronary Artery Disease, and point to the need for a heart-team based approach to support the basis of revascularization decisions, which should take into consideration the anatomical complexity, comorbidities, patient preferences and long-term health of the patient [17]. This systematic review and meta-analysis has several limitations. First, for the quantitative synthesis, the pooled estimates from published randomized trial meta- analyses were used instead of recalculating them from individual trial events, although this methodology is robust, it does not allow alternative statistical models to be explored. Second, the high degree of heterogeneity found for repeat revascularization was likely due to differences between technologies used in the PCIs (bare metal vs. first- and newer- generation drug-eluting stents) and the length of time that patients were followed post- procedure in each study. Third, a number of randomized trials included in this systematic review and meta-analysis were conducted during earlier eras of PCI and CABG. Therefore, while these earlier studies are supportive of the contemporary findings, there exists potential limitations in applying this information to current clinical practice.

It is our hope that future studies will have long-term randomized trials comparing current PCI technologies (including newer generation drug-eluting stents and intravascular imaging-guided PCI). Long-term follow up (for example, following patients longer than 10 years) is required for the determination of mortality differences and late adverse events. Future work should also include patient-centered outcomes, cost effectiveness analyses and individualized risk prediction for improved decision-making for patients with multivessel coronary artery disease.

Conclusion

According to the results of this systematic review and meta-analysis, CABG (coronary artery bypass grafting) consistently demonstrates superior clinical outcomes compared to PCI (percutaneous coronary intervention) in patients with multi-vessel coronary artery disease (CAD). Randomized trials and long-term follow-up studies consistently demonstrate that CABG reduces the all-cause mortality, MI (myocardial infarction) and the need for revascularization, demonstrating the durability and completeness of surgical revascularization therapy for high-risk population. Although there was a slight, non- significant increase in the risk of stroke associated with CABG, the overall clinical benefit of CABG greatly outweighs the negative aspects and therefore, CABG is the preferred method of choice when long-term outcomes are the priority.

The greatest benefit from CABG was seen in patients with DM (diabetes mellitus) and patients with complex coronary anatomy, i.e. patients with three-vessel disease and higher SYNTAX scores; therefore it is imperative to take into account specific anatomy of an individual patient when considering the method of intervention. The findings of this study are consistent with current international guidelines and demonstrate the value of using a multidisciplinary team approach when determining the best method for revascularization in patients with CAD. It is recommended that further research evaluates the effects of the most recent PCI technology on the long-term results of patients. Researchers should incorporate patient-centred measures into the evaluation process to create more robust treatment selection criteria, however, based on the evidence currently available, CABG should remain the treatment of choice for appropriately selected patients with multivessel coronary artery disease.

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