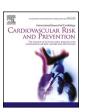
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Comparison of percutaneous coronary intervention vs coronary artery bypass graft for left main coronary artery disease in patients with prior cerebrovascular disease: A systematic review, meta-analysis and meta-regression

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ABSTRACT

Background: Previous studies suggest similar cardiovascular (CV) benefits for either percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) in patients with left main coronary artery disease (LMCAD). However, limited data exist on the influence of prior cerebrovascular disease (CEVD). Thus, we aim to compare the CV outcomes in patients with LMCAD and prior CEVD, undergoing either PCI or CABG.

Methods: A comprehensive search from (January 2000 to August 2024) identified three relevant studies. Outcomes analyzed included all-cause mortality, major adverse cardiac and cerebrovascular events (MACCE), myocardial infarction (MI), and risk of stroke in patients undergoing either PCI or CABG for LMCAD. Data analysis employed a random effects model and presented hazard ratios (HR) along with their 95 % confidence intervals (CI).

Results: Three studies involving 760 patients (361 PCI, 399 CABG) were included. PCI was associated with a significantly higher risk of MACCE (HR = 2.56; 95 % CI = 1.23–5.37; p = 0.01; I^2 = 86 %) and MI (HR = 2.97; 95 % CI = 1.72–5.13; p < 0.0001; I^2 = 0 %) compared to CABG. No significant differences were observed in all-cause mortality (HR = 1.35; 95 % CI = 0.92–1.98; p = 0.12; I^2 = 0 %) or recurrent stroke (HR = 0.83; 95 % CI = 0.40–1.70; p = 0.60; I^2 = 1 %). The risk of repeat revascularization was higher in PCI, though not statistically significant (HR = 3.44; 95 % CI = 0.50–23.60; p = 0.21; I^2 = 70 %).

Conclusion: PCI significantly elevates the risk of MACCE and MI in patients with LMCAD and prior CEVD compared to CABG. However, risks of all-cause mortality, repeat stroke, and revascularization were non-significant. Comorbidities may drive the elevated risk, underscoring the need for tailored strategies in this population.

1. Introduction

Cerebrovascular Disease (CEVD) or stroke is one of the most globally prevalent diseases, affecting 101 million people in 2019. It also resulted in 11.6 % of the total deaths, making it the second-leading cause of death

worldwide [1]. Multiple studies have established a strong association between CEVD and coronary artery disease (CAD), reporting that approximately 16.9 % of patients with CAD had prior transient ischemic attack or stroke [2,3]. Both diseases share common vascular risk factors and a similar pathophysiology, which starts with atherosclerosis. This

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may diffusely affect multiple vascular beds including coronary and carotid arteries which may explain the association mentioned above.

Patients with prior CEVD are at a higher risk of worse clinical outcomes when undergoing coronary revascularization than patients with CAD alone [4,5]. Morikami et al., in their cohort of about 15000 patients, discovered that there was a 34 % higher risk of major adverse cardiovascular events (MACE), 22 % higher risk of all-cause mortality, and 85 % higher risk of recurrent stroke in patients with stroke and CAD when compared with patients with only CAD [4]. Of the two common revascularization strategies generally adopted for CAD, percutaneous coronary intervention (PCI) is often preferred over coronary artery bypass grafting (CABG) due to its lower perioperative risk of stroke [6]. This is further reinforced by a meta-analysis that pooled 14 trials and revealed that the odds of developing a stroke are approximately 3 times higher in patients treated with CABG than in patients treated with percutaneous coronary intervention (PCI) [7]. In contrast to this, the literature reports that patients with prior CEVD have a greater risk of worse clinical outcomes after PCI due to a more extensive CAD. Such patients have a consistently higher risk of all-cause mortality and death due to a cardiac cause, and hence treatment with CABG can provide a better long-term survival [7–9]. These contrasting results make it difficult for healthcare practitioners to ascertain the optimal method of revascularization in CEVD patients.

One of the major vessels that supplies the heart with blood is the left main coronary artery (LMCA). An atherosclerotic lesion in this vessel may be considerably more dangerous as it supplies 75 %–100 % of the myocardium depending on the dominance of left coronary circulation [10]. As a result, patients suffering from LMCAD may be at a higher risk for complications. Studies support this conclusion, reporting that the risk of perioperative stroke at all time intervals of follow-up is consistently higher in patients with LMCAD than in patients with multivessel disease when undergoing CABG [11].

Multiple randomized clinical trials and meta-analyses have already been conducted to investigate the difference in clinical outcomes between PCI and CABG, however, patients with prior CEVD were excluded as they represented a high-risk population with a significantly greater likelihood of developing various adverse events. This meta-analysis aims to fill that gap in knowledge by comprehensively collecting data and giving an unbiased comparison of clinical outcomes of both revascularization strategies (PCI and CABG) in patients with prior CEVD primarily in patients of LMCAD.

2. Methods

The current systematic review and meta-analysis were performed according to Preferred reporting items for systematic review and meta-analyses (PRISMA) guidelines [12]. The protocol for this review was registered on the International Prospective Register of Systematic Reviews PROSPERO (CRD42024584442).

2.1. Data sources and search strategy

To retrieve all relevant articles, an extensive literature search was conducted on PubMed, Cochran's Central Library, and Scopus using the following search strategy with their keywords and associated MeSH terms: "(coronary artery disease OR CAD OR left main coronary artery disease OR LMCAD) AND (cerebrovascular disease OR CEVD OR stroke OR transient ischemic attack OR TIA OR carotid artery disease OR carotid stenosis OR carotid endarterectomy) AND (PCI OR percutaneous coronary intervention) AND (CABG OR coronary artery bypass graft surgery)".

In addition, we thoroughly searched the reference lists of the retrieved articles, past review articles, and meta-analyses to find any relevant studies that may have been missed in the initial search.

2.2. Study selection

The articles were selected for inclusion based on the following inclusion criteria. First, we included patients with LMCAD and prior CEVD undergoing PCI or CABG with no restriction of study type. Secondly, studies defining CEVD as any one of the following TIA, stroke, carotid artery disease, or carotid stenosis in patients with CAD undergoing PCI or CABG were included. Thirdly, all studies in the English language were included. Fourth, studies had to report the primary outcome to be included. The primary outcomes were major adverse cardiac and cerebrovascular events (MACCE) and recurrent myocardial infarction (MI).

Our exclusion criteria were as follows: case reports, review articles, editorials, and conference articles; Studies for which full articles could not be retrieved; and studies on non-human subjects.

The articles retrieved from the systematic search were exported to the EndNote Reference Library X7 software, where duplicates were screened for and removed. Two independent reviewers, H.U.H.A and A. N. evaluated the remaining articles to ensure they met the established selection criteria. Initially, articles were shortlisted based on their titles and abstracts. Those that appeared relevant underwent a full review. A third reviewer, H.A., resolved any disagreements between the reviewers.

2.3. Data extraction

The extracted data included patient demographics as well as outcome information. The patients' demographics included sample size, mean age, body mass index (BMI), hyperlipidemia, hypertension, diabetes, smokers, peripheral vascular disease, and left ventricular ejection fraction (LVEF%). Five outcomes were assessed. Firstly, the effect of CABG and PCI in patients with prior CEVD on MACCE, followed by recurrence of MI, all-cause mortality, recurrent stroke and lastly repeat revascularization.

2.4. Statistical analysis

All statistical analysis was performed on Review Manager (Version 5.4.1, Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). The outcomes were pooled using a random effects model comparing hazard ratio (HR) and corresponding 95 % confidence intervals (CI), which were calculated for the primary and secondary outcomes reported. Heterogeneity was assessed via Higgin's I² test. An I² statistic of more than 50 % was considered to have significant heterogeneity, and a value less than 50 % for I² was considered acceptable [13]. A sensitivity analyses, particularly the leave one out analysis was conducted if the heterogeneity was greater than 50 %. A p-value of less than 0.05 was considered significant. Furthermore, to explore potential sources of heterogeneity across studies, we employed the Meta Essentials tool for conducting a meta-regression analysis. This software allows for the assessment of relationships between study-level covariates (moderators) and the reported effect sizes. Moderators such as mean age, percentage of males, left ventricle ejection fraction (LVEF), smokers, peripheral artery disease (PAD), hypertension, prior MI, and diabetes mellitus were included in the analysis to determine their influence on the incidence of MI and MACCE [14].

2.4.1. Quality assessment

Quality assessment of included RCTs was conducted through the Cochrane Risk of Bias Tool [15]. The seven domains of Cochrane's tool was used in our study, which included random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases. For one observational study, the Newcastle-Ottawa Scale (NOS) was employed [16]. This scale evaluates studies based on three main criteria: selection of study groups, comparability of groups, and ascertainment of outcomes. Studies were classified as having "low," "moderate," or "high" risk of bias based on their NOS scores. Two

independent reviewers (H.U.H.A and M.H.S.) conducted the risk of bias assessment, with discrepancies resolved through consultation with a third reviewer (A.N).

3. Results

3.1. Literature search results

The PRISMA chart summarizes our literature review [Fig. 1]. The search strategy was run through three databases, providing 3567 potential articles. After removing duplicates and screening, we evaluated articles for inclusion. Our study included three studies, including two RCTs and one observational study [17–19].

3.2. Participant characteristics

A total of 760 patients with CAD and prior CEVD were included in the review, of which 361 were assigned PCI and 399 were assigned to CABG. The mean ages in the PCI and CABG groups were 67.4 and 66.7 years, respectively. Further details regarding the study and baseline characteristics are provided in (Table 1).

3.3. Results of meta-analysis

3.3.1. Risk of major adverse cardiac and cerebrovascular events (MACCE) All three studies reported data on the risk of MACCE in patients with CAD and prior CEVD undergoing PCI in comparison to CABG. Our analysis highlighted that patient who underwent PCI experienced a significantly increased risk of MACCE compared to those who underwent CABG (HR = 2.56; 95 % CI = 1.23, 5.37; p = 0.01; $I^2 = 86$ %) (Fig. 2). Furthermore, due to high heterogeneity, a sensitivity analysis was performed by excluding one study at a time, whereby the study by Yu Pan et al. was excluded resulting in a significant reduction in the risk of MACCE along with a reduction in heterogeneity from an initial value of 86 %–0 % was observed (HR = 1.73; 95 % CI 1.28, 2.35; p = 0.0004; $I^2 = 0$ %) (Supplementary Fig. 3).

3.4. Myocardial infarction (MI)

A total of two studies reported data on the risk of MI in patients with CAD and prior CEVD undergoing PCI in comparison to CABG. PCI was associated with a significantly higher risk of myocardial infarction compared to CABG (HR = 2.97; 95 % CI = 1.72, 5.13; p < 0.0001; $I^2=0$ %) (Fig. 3).

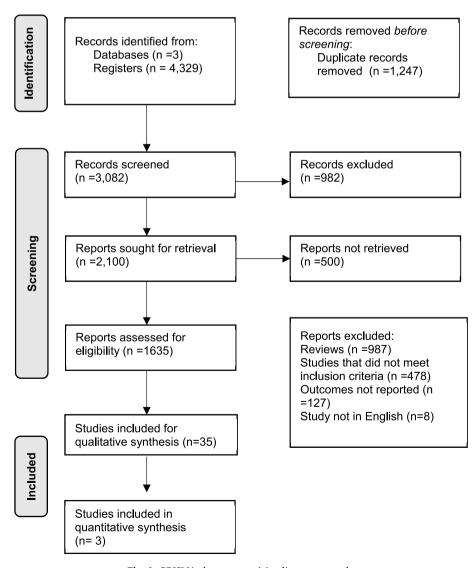


Fig. 1. PRISMA chart summarizing literature search.

Baseline characteristics of the studies included

study	Intervention	Total sample size	Intervention Total Patients Age-yrs sample size	Age-yrs		MALE (n)	<u>-</u>	Body m	Body mass index Hyperlipidemia Hypertension Diabets Mellitus	Hyperlip	idemia	Hyperten	Ision I	Diabets Mellitus	S	Current	正 ≥	History of Myocardial Infarction	_	Peripheral Artery Disease (PAD)	Peripheral Left Ventricular Artery Disease Ejection Fraction (PAD) (LVEF)	Left Ventricular Ejection Fraction (LVEF)	icular action
			PCI CABG PCI CABG PCI	PCI	CABG		CABG	CABG PCI CABG		PCI	CABG PCI	PCI C	ABG) ID	ABG P	CI	CABG PCI CABG PCI CABG PCI CABG PCI PCI	MIJ)	ABG	PCI C	CABG PCI		CABG
Diamond	PCI and	233	112 121 69.7 ± 68.3 ±	± 2.69	68.3 ±	85/	102/		28.3 27.7 ± 4.9 80/112 83/121	80/112		93/ 1	101/ 4	42/ 4	42/ 2	22/ 3	34/ 18	18/ 1	15/	38/ 36	36/ 56.	56.6 ± 55	55.5 ±
2018	CABG			9.3	8.7	112				(71.4) (68.6)		112 1	121 1	112 1	121 1	111 1	120 1	110 1	121	112 12	121 10.7		10.3
						(75.9)	(84.3)					(83.0)	(83.5)	(37.5) (34.7) (19.8) (28.3)	34.7) (19.8)	28.3) (1	(16.4) (12.4) (33.9)	12.4)		(29.8)		
Wang		253	119 134 $67.4 \pm 68.8 \pm$	$67.4 \pm$	± 8.89 ±	9.07	9.77	28.2	$27.6\pm4.4~NR$	NR			64.2	31.9	32.8	16.0	17.6 37	31.6	38.6			57.5 ± 57	$57.2 \; \pm$
2021				9.8	8.8	(84)	(104)	± 4.8				(92)] (98)	[38]	(44)	[19]	[23]	[37]	(21)	[29]	[33] 12.8		13.4
Yu Pang		274	130 144	65	63	108	119	NR		26	38	106 1	120 4								9 (6.3) 59	59	6
2021				(58-73)	(58-73) (55-74) (83.1) ((83.1)	(82.6)			(20.0)	(26.4)	(81.5) (83.3) (32.3) (27.8) (45.4) (50.7) (30.8) (29.9) (10.0)	83.3) (32.3) (27.8) (45.4) (50.7) (3	30.8)	29.9)	(10.0)	(45	(45–68) (46–67)	46-67

3.5. All-cause mortality

All three studies reported data on all-cause mortality. Our analysis highlighted a non-significant difference in reducing the risk of all-cause mortality between the PCI and CABG (HR = 1.35; 95 % CI = 0.92, 1.98; $p=0.12;\, I^2=0$ %) (Fig. 4).

3.6. Recurrent stroke

All three studies reported data on the risk of recurrent stroke. Our analysis highlighted a non-significant difference in reducing the risk of recurrent stroke between the PCI and CABG (HR = 0.83; 95 % CI = 0.40, 1.70; p = 0.60; I² = 1 %) (Fig. 5).

3.7. Repeat revascularization

The risk of repeat revascularization was higher in patients undergoing PCI, although this increase was statistically non-significant (HR = 3.44; 95 % CI 0.50, 23.60; P = 0.21; I² = 70 %) (Fig. 6). Due to high heterogeneity, a leave-one-out analysis was conducted, excluding the study by Yu Pan. This exclusion led to a non-significant increase in the risk of and decreased heterogeneity, with the $\rm I^2$ value dropping from 70 % to 0 %. The updated risk estimate for repeat revascularization was HR = 1.34, 95 % CI 0.41, 4.42; P = 0.63; $\rm I^2 = 0$ %) (Supplementary Fig. 4).

3.7.1. Regression

The meta-regression analysis for MI did not identify any significant associations with the examined covariates. Specifically, the mean age (coefficient: -0.18, p-value: 0.852), percentage of males (coefficient: -0.69, p-value: 0.474), LVEF (coefficient: 0.44, p-value: 0.648), percentage of current smokers (coefficient: -0.20, p-value: 0.837), percentage of patients with peripheral artery disease (PAD) (coefficient: -0.31, p-value: 0.747), percentage of patients with hypertension (coefficient: -0.92, p-value: 0.338), percentage of patients with prior MI (coefficient: 0.92, p-value: 0.339), and percentage of patients with DM (coefficient: −0.57, p-value: 0.554) did not significantly impact the risk of MI. Similarly, the meta-regression analysis for MACCE also showed no significant relationships with the variables assessed. The mean age (coefficient: -0.87, p-value: 0.560), percentage of males (coefficient: 0.14, p-value: 0.925), mean LVEF (coefficient: 0.98, p-value: 0.511), percentage of current smokers (coefficient: 0.60, p-value: 0.686), percentage of patients with PAD (coefficient: -0.94, p-value: 0.530), percentage of patients with hypertension (coefficient: -0.19, p-value: 0.900), percentage of patients with prior MI (coefficient: 0.80, p-value: 0.595), and percentage of patients with DM (coefficient: -1.00, p-value: 0.504) did not significantly affect the risk of MACCE. Results for all meta-regression analyses are represented in Supplementary Table 3. Scatter plots are presented in the Supplementary Figs. 6–20.

3.7.2. Risk of bias

All studies included in this meta-analysis exhibited a consistently low risk of bias. Notably, both RCTs [17,18] were deemed to have a low risk of bias across all evaluated domains. The observational study by Yu Pan et al. (2021) [19] received a total score of 7 on the NOS, signifying its high quality and suitability for inclusion in this analysis. Detailed assessments of bias risk are provided in Supplementary Figures 1 and 2 and Table 1.

4. Discussion

This meta-analysis demonstrates that PCI is associated with a significantly higher risk of MACCE and MI compared to CABG in patients with LMCAD and prior CEVD. However, there were no significant differences in all-cause mortality, repeat stroke, or revascularization between the two interventions.

LMCAD is characterized by significant obstruction of the left main

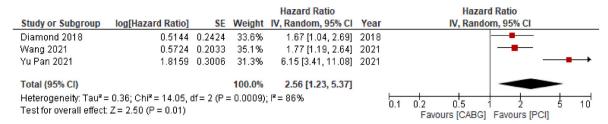


Fig. 2. Comparison of PCI vs CABG on risk of major adverse cardiac and cerebrovascular events (MACCE). Hazard ratio (HR), standard Error (SE), 95 % confidence interval (CI), and I^2 statistics.

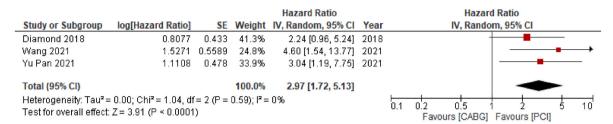


Fig. 3. Comparison of PCI vs CABG on risk of recurrent myocardial infarction. Hazard ratio (HR), standard Error (SE), 95 % confidence interval (CI), and I² statistics.

				Hazard Ratio		Hazard Ratio
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Diamond 2018	0.237	0.3486	30.9%	1.27 [0.64, 2.51]	2018	
Wang 2021	0.1587	0.2853	46.1%	1.17 [0.67, 2.05]	2021	-
Yu Pan 2021	0.6745	0.4036	23.0%	1.96 [0.89, 4.33]	2021	-
Total (95% CI)			100.0%	1.35 [0.92, 1.98]		.
Heterogeneity: Tau² = Test for overall effect:	The second secon	= 2 (P =	0.57); I² =	: 0%		0.1 0.2 0.5 1 2 5 10 Favours [CABG] Favours [PCI]

Fig. 4. Comparison of PCI vs CABG on risk of all-cause mortality. Hazard ratio (HR), standard Error (SE), 95 % confidence interval (CI), and I² statistics.

				Hazard Ratio		Hazard Ratio
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Diamond 2018	0.3488	0.5419	45.8%	1.42 [0.49, 4.10]	2018	
Wang 2021	-0.4747	0.6327	33.7%	0.62 [0.18, 2.15]	2021	
Yu Pan 2021	-0.9315	0.8134	20.5%	0.39 [0.08, 1.94]	2021	•
Total (95% CI)			100.0%	0.83 [0.40, 1.70]		
Heterogeneity: Tau ^z = Test for overall effect:	The second control of	= 2 (P =	0.36); l² =	1%		0.1 0.2 0.5 1 2 5 10 Favours [CABG] Favours [PCI]

Fig. 5. Comparison of PCI vs CABG on risk of recurrent stroke. Hazard ratio (HR), standard Error (SE), 95 % confidence interval (CI), and I^2 statistics.

				Hazard Ratio		Hazard Ratio	
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Random, 95% CI		IV, Random, 95% CI	
Diamond 2018	0.077	1.0072	31.7%	1.08 [0.15, 7.78]			
Wang 2021	0.4187	0.7641	36.9%	1.52 [0.34, 6.80]		- • -	
Yu Pan 2021	3.3714	1.0258	31.3%	29.12 [3.90, 217.44]			→
Total (95% CI)			100.0%	3.44 [0.50, 23.60]			
Heterogeneity: Tau² = Test for overall effect:	the same of the sa	= 2 (P =	0.03); l²=	70%	0.01	0.1 1 10 1 Favours [PCI] Favours [CABG]	00

Fig. 6. Comparison of PCI vs CABG on risk of repeat revascularization. Hazard ratio (HR), standard Error (SE), 95 % confidence interval (CI), and I² statistics.

coronary artery, which is critical for supplying blood to a substantial portion of the myocardium [20]. This obstruction increases the risk of severe ischemia and MI, making effective and durable revascularization strategies essential. Patients with LMCAD often have comorbid conditions such as hypertension, diabetes, and hyperlipidemia, which complicate treatment decisions and affect clinical outcomes. A study

found that the 10-year mortality rate with just LMCAD was significantly worse than those of three arteries [21]. It is crucial to consider that these patients frequently present with both CAD and peripheral vascular disease [22]. The shared pathophysiological mechanisms, such as atherosclerosis and vascular stiffness, contribute to this complexity [23]. Additionally, atrial fibrillation associated with CAD may further

exacerbate the risk of cardioembolic strokes, a form of CEVD [24]. The gap in the literature regarding patients with concurrent CEVD and LMCAD underscores the importance of this meta-analysis. Many studies exclude CEVD patients, leading to uncertainty in treatment decisions [23] While CABG is generally effective, it carries a stroke risk of 0.0 %-5.2 %, influenced by various factors such as patient characteristics and surgical techniques [25-27]. Conversely, PCI, though less invasive, may be linked to higher rates of recurrent cerebrovascular events, MI, and death in patients with prior strokes [28,29]. Current guidelines from cardiovascular societies like the European Society of Cardiology/European Association for Cardio-Thoracic Surgery (ESC/EACTS) and American College of Cardiology/American Heart Association (ACC/AHA) recommend CABG for LMCAD, especially in patients with complex coronary anatomy or high SYNergy between PCI with TAXus and Cardiac Surgery (SYNTAX) scores, due to its superior long-term outcomes [30]. PCI is considered a viable alternative for those with lower SYNTAX scores or higher surgical risk. However, there is limited guidance for patients with concurrent CEVD, leaving clinicians with insufficient direction on balancing stroke risks between PCI and CABG in this high-risk group [30]. This systematic review and meta-analysis aim to fill this gap by comparing PCI and CABG outcomes specifically in LMCAD patients with prior CEVD. Previous meta-analyses have shown that PCI and CABG are similarly effective regarding mortality, MI, and stroke, but PCI has a higher repeat revascularization rate [31-36]. Our analysis provides crucial insights for optimizing treatment strategies and guiding clinical decisions in this challenging patient population.

Our analysis demonstrates that PCI is associated with a higher risk MI and MACCE compared to CABG in patients with LMCAD and CEVD. This increased risk likely reflects the need for more comprehensive revascularization, which CABG achieves more effectively. By bypassing multiple obstructed arteries simultaneously and leveraging the long-term durability of arterial grafts, CABG provides superior revascularization outcomes. In contrast, PCI may exacerbate preexisting vascular disease through inflammatory responses and stent-related complications, positioning CABG as the safer option for reducing ischemic events and ensuring long-lasting benefits [37].

CABG further minimizes complications such as restenosis and stent thrombosis, which are particularly problematic in patients with significant vascular burden. Additionally, its ability to deliver stable and durable blood flow is especially advantageous for individuals with impaired cerebral circulation due to prior CEVD, offering better protection against both cardiac and cerebrovascular events [30].

Despite these findings, our analysis revealed no significant difference between PCI and CABG in terms of all-cause mortality, repeat stroke, or repeat revascularization in patients with LMCAD and CEVD. Stroke risk following CABG, however, depends significantly on whether the procedure is performed on-pump or off-pump. On-pump CABG, which involves the use of a cardiopulmonary bypass machine, requires manipulation of the aorta—a process that can dislodge atheromatous plaques and increase the risk of embolic events and perioperative stroke [38]. In contrast, off-pump CABG eliminates the need for aortic manipulation, significantly reducing the risk of embolization and perioperative stroke [39].

Patients with prior cerebrovascular events, such as transient ischemic attacks (TIA) or strokes, exhibit superior outcomes with off-pump CABG compared to the on-pump approach. Off-pump CABG has been associated with a lower incidence of stroke, delirium, and other adverse postoperative neurological outcomes in these high-risk patients [40]. For those with heightened neurological risk, off-pump CABG provides a clear advantage, reducing the likelihood of postoperative complications and making it the preferred surgical strategy.

In our analysis, the impact of off-pump CABG was partially addressed in two included studies. Diamond et al. reported that 28.6 % (34/119) of CABG patients underwent off-pump surgery, while Wang et al. reported a lower rate of 16.5 %. However, Yu Pang et al. did not specify the proportion of off-pump procedures, limiting our ability to

comprehensively assess its influence across the included cohorts. This lack of detailed reporting may explain why our analysis did not find CABG to be superior to PCI in terms of stroke risk, as the majority of CABG patients in the included studies underwent on-pump surgery.

These findings highlight that prior CEVD should not be the main reason to favor PCI over CABG. Instead, factors like the complexity of the coronary anatomy, SYNTAX score, the likelihood of achieving complete revascularization, and the patient's preferences should be carefully evaluated. These considerations should guide the selection of the most appropriate revascularization procedure for each case.

This meta-analysis is the first to compare revascularization strategies in patients with LMCAD and CEVD, addressing a critical gap in the current literature. Our regression analysis yielded consistent findings across key covariates such as age, gender, and comorbidities. However, several limitations must be acknowledged. Notably, one of the studies included participants with both LMCAD and other forms of CAD, which may have introduced heterogeneity into our results [18]. Additionally, we included a single observational study by Pan et al. [19], which, unlike RCTs, is more vulnerable to bias and confounding factors. The observational nature of this study introduces potential biases that should be considered when interpreting the findings. Selection bias was a concern due to the non-random assignment of treatment, which may have led to confounding by indication, as decisions to perform PCI or CABG could have been influenced by patient characteristics such as comorbidities or disease severity. Furthermore, measurement bias was present due to inconsistent data collection, including the absence of key variables like the SYNTAX score, as well as variability in follow-up durations, which could lead to misclassification of outcomes. Confounding bias remained as well due to unmeasured factors, such as disease severity and clinical judgment, which were not fully adjusted for in the

Despite these biases, the inclusion of this observational study had minimal impact on the heterogeneity of most outcomes. There is evidence suggesting that observational studies can complement RCT data by improving the external validity of findings, particularly when RCTs are scarce or have stringent eligibility criteria. Empirical reviews have also shown that meta-analyses of observational studies often yield effect estimates comparable to those from RCTs. Thus, while this mixed approach introduces inherent heterogeneity, we believe it strengthens the comprehensiveness of our analysis [46]. In line with this, its exclusion in our analysis notably reduced the heterogeneity observed for events MACCE and repeat revascularization, while maintaining the overall effect size, suggesting that the results from this study were reliable. The high heterogeneity observed in MACCE outcomes is likely due to differences in the definitions and measurements of MACCE, as well as variability in revascularization techniques across the Pan et al. study, making direct comparisons challenging. These factors should be carefully considered when interpreting our findings.

5. Conclusion

CABG demonstrates a significant advantage over PCI in reducing the risk of MACCE and MI in patients with LMCAD and prior CEVD. Both interventions show similar outcomes for all-cause mortality, repeat stroke, and repeat revascularization, challenging the notion that PCI is preferentially recommended in this patient population due to concerns about stroke risk. These findings indicate that treatment decisions should consider coronary anatomy, SYNTAX score, and individual patient factors. Further research is needed to explore long-term effects and refine clinical guidelines for this high-risk population.

CRediT authorship contribution statement

Muhammad Hamza Shuja: Writing – review & editing, Writing – original draft, Conceptualization. **Firzah Shakil:** Project administration, Methodology, Investigation, Conceptualization. **Syed Hassaan Ali:**

Project administration, Methodology. Qazi Shurjeel Uddin: Validation, Supervision. Ayesha Noman: Supervision, Software, Resources. Javed Iqbal: Funding acquisition, Conceptualization. Muhammad Ahmed: Software. Faiza Sajid: Visualization, Validation. Haya Waseem Ansari: Writing – original draft, Visualization. Syed Ahmed Farhan: Resources. Huzaifa Ul Haq Ansari: Supervision, Software. Syed Husain Farhan: Resources, Project administration. Muhammad Moiz Nasir: Methodology, Investigation. Sana Qazi: Formal analysis, Data curation. Muhammad Majid: Validation, Supervision, Software.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcrp.2025.200370.

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