Neurological outcomes postcoronary artery bypass graft on-pump versus off-pump meta-analysis

Original Article

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ABSTRACT

Introduction: Coronary artery disease is the primary cause of mortality and a significant public health concern. Numerous treatments exist, such as coronary artery bypass graft (CABG), which combines two methods: small thoracotomy and sternotomy. Several methods have been devised to enhance the results of surgery, such as using a circulation machine (on-pump) or off-pump.

Objective: To ascertain if neurological results from off-pump and on-pump CABG actually vary in any way.

Patients and Methods: The current study is a meta-analysis including randomized controlled trials and retrospective, prospective, and observational studies evaluating and comparing neurological outcomes between on-pump and off-pump on patients undergoing CABG.

Results: The individual odds ratios (OR) favor off-pump CABG, indicating a lower risk of stroke compared to on-pump CABG. It was noted that there were significant differences in the incidence of transient ischemic attacks between on-pump and off-pump CABG procedures. OR of 0.40 [95% confidence interval (CI): 0.10, 1.62], indicating a lower, though not statistically significant, risk of transient ischemic attacks in the off-pump group. Cognitive impairment. It was reported a slightly lower incidence of cognitive impairment in off-pump patients (0.70%) compared to on-pump patients (0.83%), along with stroke rates of 1.34% for off-pump versus 1.54% for on-pump. It was reported a significant reduction in cognitive impairment for off-pump procedures, with an OR of 0.46 (95% CI: 0.28, 0.77). The overall pooled OR from the random-effects model is 0.51 (95% CI: 0.38, 0.67), suggesting that off-pump CABG is associated with approximately a 49% reduction in the risk of cognitive impairment compared to on-pump CABG.

Data sources: Medline databases (PubMed, Medscape, ScienceDirect, and EMF-Portal) and all materials available on the internet till 2022.

Conclusion: Based on our study result, it was estimated that off-pump CABG is associated with a lower incidence of neurological complications than on-pump CABG.

Key Words: Cardiopulmonary bypass, coronary artery bypass graft surgery, coronary artery disease, transient ischemic attack.

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INTRODUCTION

Cardiopulmonary bypass (CPB), which exposes the blood to a non-physiological environment (extracellular circulation), can be used during coronary artery bypass graft surgery (CABG), or it can be done on a beating heart with or without CPB assistance[1]. Blood interaction with nonendothelial circuit chemicals stimulates the activation of coagulation pathways, complement components, and a cellular immunological response, which results in cellular damage and subsequent organ destruction. Extracorporeal circulation also typically produces a systemic inflammatory response.

Off-pump CABG prevents the possible pump consequences, such as embolic accidents, lung injury, renal failure, endocrine, metabolic, and cellular inflammatory reactions of CPB, as well as effects on the liver, viscera, and neurological system[2]. When compared to on-pump CABG, the potential advantages of off-pump CABG depend on avoiding CPB and requiring less aortic manipulation. Compared to on-pump CABG, off-pump CABG had better short-term results but worse long-term results[3].

Higher rates of early graft failure and the possibility of inadequate cardiac revascularization are the reasons for this. On the other hand, individuals with a positive history of cerebrovascular illness may benefit from off-pump coronary surgery, as shown by the potential correlation between off-pump CABG and a lower risk of postoperative stroke and increased benefits in high-risk patients[4].

An acute inflammatory reaction is linked to CPB. According to Ali *et al.*[5], this reaction causes a slight to a

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significant shift in interstitial fluid, an immediate, enormous defensive reaction, and a variety of microemboli.

After CABG, neurological damage is a significant side effect. There are two varieties. Type 1 comprises coma (incidence 3–6%), stroke, and transient ischemic attack (TIA). More subdued, type 2 involves cognitive impairment. These are deficits linked to motor function, mental reactions, attention, focus, and memory[6].

Aim

The current meta-analysis aims to determine if there is any real difference between off-pump and on-pump CABG in terms of neurological outcomes.

PATIENTS AND METHODS:

Type of study

It is a systematic review and meta-analysis considered randomized controlled trials and retrospective or prospective observational studies evaluating and comparing neurological outcomes between on-pump and off-pump CABG.

Types of participants

This review considered studies reporting population comprised of patients undergoing CABG.

Types of intervention

Interventions of interest included those related to on-pump and off-pump as the main technique for ischemic heart patients undergoing CABG.

Types of outcome measure

The primary outcome of interest is reviewing and comparing neurological outcomes between on-pump and off-pump CABG, such as postoperative stroke (transient or permanent), delirium requiring pharmacological treatment or a combination of both, collectively defined "major adverse neurological events."

Search strategy for identification of studies

The search plan took into account the availability of both manual and electronic data. Up to 2023, databases from PubMed, EMbase, CINAHL, and the Cochrane database were searched electronically. The following Medical Subject Heading (MeSH) terms were used in the search: "coronary artery bypass, off-pump" OR "off-pump coronary artery bypass" OR "off-pump" OR "coronary artery bypass, beating heart" OR "beating heart cardiopulmonary bypass" OR "cardiopulmonary bypass" OR "bypass, cardiopulmonary") AND "randomized controlled trial" OR "clinical trial" OR "controlled clinical trials, randomized" OR "trials, randomized clinical" OR "prospective," OR "observesional study," OR "retrospective study" AND (neurological outcomes).

Additionally, complete copies of articles from accessible medical journals and other published studies found through searches were obtained for data synthesis. These were also discussed with a number of investigators who are experts in the field and published case reports that met the inclusion criteria based on their title, abstract, and subject descriptors. We limited the scope of our review to English-language studies.

Reviews and research involving animals were not included. Excluded from consideration were studies without any of the intended outcome indicators and people treated with alternative modalities, such as emergency or salvage circumstances or percutaneous coronary intervention. Complete data was not included. Excluded from consideration were studies that compared on-pump versus off-pump CABG procedures.

Methods of the review

Locating and selecting studies

Abstracts of articles identified using the search strategy above were viewed, and articles that appeared to fulfill the inclusion criteria were retrieved in full. Data on at least one of the outcome measures must be included in the study.

Data extraction

Data was independently extracted by two reviewers and cross-checked.

Statistical consideration

When calculating quantitative data, the data produced by each included randomized controlled trial was used to compute the odds ratio (OR; for categorical outcome data) or the standardized mean differences (for continuous data), along with their 95% confidence intervals (CIs). Using Review Manager software from the Cochrane Collaboration results from similar groupings of trials were aggregated into statistical meta-analyses when suitable, given the available data. The conventional χ^2 test was used to assess heterogeneity among the pooled studies. Given the notable variations in the impact measure between the studies under comparison, a random effect analysis utilizing the protocol outlined by DerSimonian and Laird[7] was conducted. The interstudy variance is explained by the random effect analysis. We shall provide the random effect analysis findings even in the absence of substantial heterogeneity due to the poor power of the homogeneity test.

All statistical analyses for pooling the studies were performed on the STATA statistical Software, release 14.0 (Stata Crop. 2015, College Station, Texas, USA).

Statistical analysis

Statistical analysis was performed with Open Meta (analyst) package for the meta-analysis. A grouped random-effects model was used to calculate the pooled mean outcome and create forest plots to display the individual study means of the two modalities to account for varying true effect sizes of the studies. A random-effects model was chosen to allow for the generalization of conclusions beyond the studies included in the analysis[8]. I^2 was used to assess heterogeneity.

RESULTS:

Study selection

The initial search yielded 36 results, out of which 26 were excluded, resulting in 10 studies included in the final quantitative synthesis. These included studies encompass a range of study designs, including retrospective analyses, randomized controlled trials, and prospective randomized studies. The general characteristics of the included studies are shown in (Fig. 1).

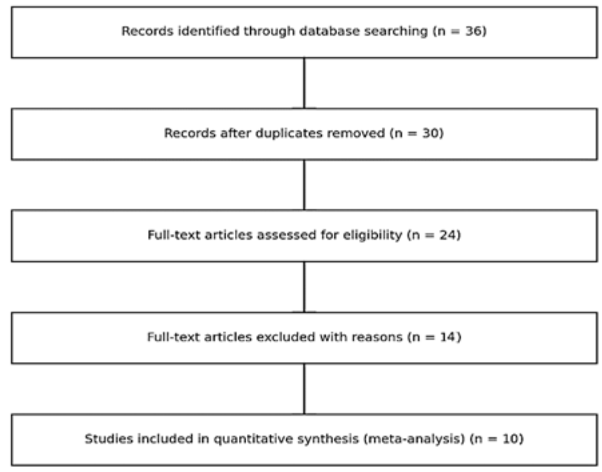

Fig. 1: Flow diagram of the literature search and study selection processes.

Table 1: General characteristics of the included studies

References	Year	Study type	Sample size
Yokoyama *et al.*[9]	2000	Retrospective analysis	725 (242 off-pump, 483 on-pump)
Abraham *et al.*[10]	2001	Retrospective	1227 (973 on-pump, 254 off-pump)
Magee *et al.*[11]	2001	Retrospective	9965 (2891 diabetic, 7074 nondiabetic; 1175 off-pump, 8790 on-pump)
Sisillo *et al.*[12]	2007	Retrospective	8002 (1415 off-pump, 6587 on-pump)
Marasco *et al.*[13]	2008	Retrospective	892 (446 off-pump, 446 on-pump)
Naseri *et al.*[14]	2009	Prospective randomized study	120 (60 off-pump, 60 on-pump)
Emmert *et al.*[15]	2011	Retrospective analysis	1015 (540 off-pump, 475 on-pump)
Lemma *et al.*[16]	2012	Randomized controlled trial	411 (203 on-pump, 208 off-pump)
Ji *et al.*[17]	2014	Retrospective	485 (282 off-pump, 203 on-pump)
Dominici *et al.*[6]	2020	Retrospective Observational study	414 (295 on-pump, 119 off-pump)

The retrospective analyses included studies by Abraham *et al*.[10] with 1227 participants, Sisillo *et al*.[12] with 8002 participants, Ji *et al*.[17] with 485 participants, Magee *et al*.[11] with 9965 participants, Dominici *et al*.[6] with 414 participants, Emmert *et al*.[15] with 1015 participants, Yokoyama *et al*.[9] with 725 participants, Marasco *et al*.[13] with 892 participants, and a second study by Magee *et al*.[11] focusing on diabetic patients with 346 participants. The randomized controlled trial included Lemma *et al*.[16] with 411 participants, and the prospective randomized study included Naseri *et al*.[14] with 120 participants. These studies collectively provide a robust dataset for evaluating the impact of off-pump versus on-pump CABG on neurological outcomes such as stroke, delirium, and cognitive impairment (Table 1).

Cerebral strokes

This meta-analysis explores neurological outcomes, particularly stroke, following on-pump versus off-pump CABG surgery across several studies. Abraham *et al*.[10] found a stroke incidence of 3.6% in on-pump patients versus 1.2% in off-pump patients, although the reduction was not statistically significant. Lemma *et al*.[16] observed no strokes in the off-pump group compared to a 0.5% incidence in the on-pump group, alongside a lower composite of adverse outcomes. Sisillo *et al*.[12] reported on a large sample and found no significant differences in stroke rates or immediate postoperative outcomes between the two groups. Ji *et al*.[17] noted that off-pump CABG was associated with reduced complication rates. Yokoyama *et al*.[9] reported a lower incidence of neurological complications, including stroke (3.3 vs. 5%), for off-pump procedures. Magee *et al*.[11] highlighted that off-pump CABG reduced stroke rates in diabetic and nondiabetic patients. Naseri *et al*.[14] showed significantly fewer strokes (0 vs. 3.4%) and better neurological scores postoperation in the off-pump group. Dominici *et al*.[6] found lower postoperative stroke rates (3.4 vs. 9.8%) and delirium in off-pump patients with previous cerebrovascular events. Emmert *et al*.[15] corroborated these findings with stroke rates of 0.7% in off-pump versus 2.3% in on-pump patients. Overall, off-pump CABG consistently demonstrates a trend towards reduced neurological complications, including stroke, when compared to on-pump CABG, although heterogeneity and varying study designs necessitate cautious interpretation of these results.

The individual OR mostly favor off-pump CABG, indicating a lower risk of stroke compared to on-pump CABG. For instance, Abraham *et al*.[10] reported an OR of 0.32 (95% CI: 0.10, 1.05), and Magee *et al*.[11] reported a significant reduction with an OR of 0.07 (95% CI: 0.03, 0.20). The overall pooled OR from the random-effects model is 0.43 (95% CI: 0.24, 0.76), suggesting that off-pump CABG is associated with a 57% reduction in stroke risk compared to on-pump CABG. The common effect model supports this with an OR of 0.48 (95% CI: 0.37, 0.62). However, there is substantial heterogeneity among the studies (I2=70%, *P<0.01*), indicating variability in the results. Despite this heterogeneity, the overall trend clearly favors off-pump CABG in reducing stroke incidence, highlighting its potential benefit in improving neurological outcomes (Fig. 2).

Study	Events (Off-Pump)	Total (Off-Pump)	Events (On-Pump)	Total (On-Pump)	OR	95% CI
Reginald Abraham et al.	3	254	35	973	0.32	[0.10; 1.05]
Various (2016)	0	208	1	203	0.32	[0.01; 7.99]
Erminio Sisillo et al.	19	1415	101	6587	0.87	[0.53; 1.43]
Qiang Ji et al.	4	203	6	282	0.92	[0.26; 3.32]
Taro Yokoyama et al.	8	483	16	725	0.75	[0.32; 1.76]
Mitchell J. Magee et al.	4	8790	45	7074	0.07	[0.03; 0.20]
Erminio Sisillo et al.	19	1415	101	6587	0.87	[0.53; 1.43]
Mohammad Hassan Naseri et al.	0	60	2	60	0.19	[0.01; 4.11]
Dominici et al.	4	119	29	295	0.32	[0.11; 0.93]
Emmert et al.	9	540	30	475	0.25	[0.12; 0.54]
Common effect model		**13487**		**23261**	**0.48**	**[0.37; 0.62]**
Random effects model					**0.43**	**[0.24; 0.76]**
Heterogeneity: $I^2 = 70\%$, $\tau^2 = 0.5243$, $p < 0.01$						

Fig. 2: Forest plot of random effect model of cerebral strokes among included studies.

Transient ischemic attacks

Studies by Naseri *et al*.[14] and Yokoyama *et al*.[9] highlight significant differences in the incidence of TIA between on-pump and off-pump CABG procedures. Naseri *et al*.[14] reported that TIA occurred in 5% of off-pump patients compared to 15.3% of on-pump patients, indicating a substantial reduction in TIA incidence with off-pump CABG. Yokoyama *et al*.[9] also noted a decrease in neurological complications, including TIA, in the off-pump group. These findings suggest that off-pump CABG is associated with a significantly lower risk of TIA compared to the on-pump approach, making it a potentially safer option for reducing this specific neurological complication.

Naseri *et al*.[14] reported an OR of 0.40 (95% CI: 0.10, 1.62), indicating a lower, though not statistically significant, risk of TIA in the off-pump group. Yokoyama *et al*.[9] found an OR of 0.52 (95% CI: 0.19, 1.40), also suggesting a reduced but not statistically significant TIA risk for off-pump CABG. The overall pooled OR from the random-effects model is 0.47 (95% CI: 0.21, 1.07), suggesting that off-pump CABG potentially reduces the risk of TIA by about 53% compared to on-pump CABG, though this finding is not statistically significant. The heterogeneity is low (I2=0%, *P=0.77*), indicating consistent results across the studies. These findings suggest a trend toward a lower incidence of TIA with off-pump CABG, but further studies with larger sample sizes are needed to confirm this potential benefit (Fig. 3).

Study	Events (Off-Pump)	Total (Off-Pump)	Events (On-Pump)	Total (On-Pump)	OR	95% CI
Mohammad Hassan Naseri et al.	3	60	7	60	0.40	[0.10; 1.62]
Yokoyama et al.	5	242	19	483	0.52	[0.19; 1.40]
Common effect model		**302**		**543**	**0.47**	**[0.21; 1.07]**
Random effects model					**0.47**	**[0.21; 1.07]**
Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.77$						

Fig. 3: Forest plot of random effect model of transient ischemic attacks among included studies.

Cognitive impairment

The studies by Magee *et al*.[11], Sisillo *et al*.[12], and Marasco *et al*.[13] provide insights into cognitive impairment and other neurological outcomes following on-pump versus off-pump CABG procedures. Sisillo *et al*.[12] reported a slightly lower incidence of cognitive impairment in off-pump patients (0.70%) compared to on-pump patients (0.83%), along with stroke rates of 1.34% for off-pump versus 1.54% for on-pump. Despite these findings, no significant difference in overall neurological outcomes was observed. Marasco *et al*.[13] reviewed general neurocognitive outcomes across multiple studies with a combined sample size of 892. Magee *et al*.[11] focused on diabetic patients and reported data for 346 off-pump and 2545 on-pump cases with a significant lower incidence of cognitive impairment in the off-pump group. Overall, the evidence suggests a trend towards slightly lower cognitive impairment rates with off-pump CABG, but significant factors such as preoperative risk and renal impairment must be considered when evaluating neurological outcomes.

Sisillo *et al*.[12] reported an OR of 0.85 (95% CI: 0.43, 1.66), indicating no significant difference in cognitive impairment between the two groups. Marasco *et al*.[13] found a significant reduction in cognitive impairment with off-pump CABG, with an OR of 0.45 (95% CI: 0.31, 0.66). Magee *et al*.[11] also reported a significant reduction in cognitive impairment for off-pump procedures, with an OR of 0.46 (95% CI: 0.28, 0.77). The overall pooled OR from the random-effects model is 0.51 (95% CI: 0.38, 0.67), suggesting that off-pump CABG is associated with approximately a 49% reduction in the risk of cognitive impairment compared to on-pump CABG. The heterogeneity is low (I2=25%, *P=0.26*), indicating consistent results across the studies. These findings collectively suggest a significant benefit of off-pump CABG in reducing cognitive impairment relative to the on-pump approach (Fig. 4).

Study	Events (Off-Pump)	Total (Off-Pump)	Events (On-Pump)	Total (On-Pump)	OR	95% CI
Erminio Sisillo et al.	10	1415	55	6587	0.85	[0.43; 1.66]
Marasco et al.	45	446	89	446	0.45	[0.31; 0.66]
Magee et al.	17	346	255	2545	0.46	[0.28; 0.77]
Common effect model		**2207**		**9578**	**0.50**	**[0.38; 0.67]**
Random effects model					**0.51**	**[0.38; 0.67]**

Heterogeneity: $I^2 = 25\%$, $\tau^2 < 0.0001$, $p = 0.26$

Fig. 4: Forest plot of random effect model of cognitive impairment among included studies.

DISCUSSION

Globally, coronary artery disease is the primary cause of mortality and a significant public health concern. It is among the most prevalent reasons to consider surgery. Numerous procedures exist, such as CABG, which combines two approaches: mini-thoracotomy and sternotomy. A variety of methods have been devised to enhance the results of surgery, such as using an extracorporal circulation machine (on-pump or off-pump)[18].

CPB is used in on-pump CABG to create a quiet, bloodless surgical field; however it comes with a number of postoperative problems and a systemic inflammatory reaction. In an effort to lower these hazards, off-pump CABG was developed, and it has demonstrated promise in lowering transfusion rates, early morbidity, ICU stays, and surgery times. Nonetheless, there is ongoing debate on the efficacy of off-pump CABG; while some studies have shown promising results, others have raised doubts[19]. Therefore, the purpose of this study was to ascertain whether there is a meaningful distinction in neurological outcomes between off-pump and on-pump CABG. In order to ascertain whether there is a true difference in neurological outcomes between off-pump and on-pump CABG, a meta-analysis of observational studies and randomized controlled trials assessing and contrasting neurological outcomes between off-pump and on-pump CABG patients is being conducted.

About the overall features of the studies that are included. According to the current study, the retrospective analyses comprised studies by Abraham *et al*.[10] with 1227 participants, Sisillo *et al*.[12] with 8002 participants, Ji *et al*.[17] with 485 participants, Magee *et al*.[11] with 9965 participants, Dominici *et al*.[6] with 414 participants, Emmert *et al*.[15] with 1015 participants, Yokoyama *et al*.[9] with 725 participants, Marasco *et al*.[13] with 892 participants and a second study by Magee *et al*.[11] with 346 participants that focused on diabetic patients. Lemma *et al*.[16], an randomized controlled trial with 411 participants, and Naseri *et al*.[14], a prospective randomized trial, were both included. Involving 120 people. Together, these investigations offer a strong dataset that may be used to compare the effects of on-pump and off-pump CABG on neurological outcomes, including delirium, stroke, and cognitive decline.

Wang *et al*.[20] conducted a meta-analysis on 11 chosen papers, comprising two randomized control trials and nine observational studies. The analysis comprised 6741 patients in total, 2348 of whom were receiving off-pump CABG and 4393 of whom were getting on-pump CABG. In the chosen studies, there was no evidence of heterogeneity (I2=0.0%, *P=0.544*).

In this regard, Sá *et al*.[19] calculated that 13 524 patients, spanning the years 2000–2012, were examined, 6758 of whom underwent off-pump CABG and 6766 of whom underwent on-pump CABG. They noted that the majority of the studies included patients with mean ages in the sixth decade of life, the majority of whom were male, on-pump CABG patients, and who had greater mean coronary bypass grafts. There was a moderate risk of bias in the overall internal validity.

This meta-analysis compares the neurological outcomes – particularly stroke – of CABG surgery performed on-pump versus off-pump using data from many studies. Stroke incidence was 3.6% in on-pump patients compared to 1.2% in off-pump patients, according to Abraham *et al*.[10], although the difference was not statistically significant. Lemma *et al*.[16] found a reduced composite of unfavorable outcomes and no strokes in the off-pump group compared to a 0.5% incidence in the on-pump group. According to Sisillo *et al*.[12], who examined a sizable sample, there were no appreciable variations between the two groups' immediate postoperative results or stroke rates. According to Ji *et al*.[17], there was a lower incidence of complications with off-pump CABG. The Yokoyama *et al*.[9] group found that off-pump surgeries had a reduced incidence of neurological consequences, such as stroke (3.3 vs. 5%). Off-pump CABG lowered stroke rates in both diabetic and nondiabetic patients, according to Magee *et al*.[11]. According to Naseri *et al*.[14], the off-pump group had improved neurological ratings following surgery and a substantial decrease in strokes (0 vs. 3.4%). Dominici *et al*.[6] observed that among off-pump patients with prior cerebrovascular episodes, there was a reduced incidence of delirium and postoperative stroke (3.4 vs. 9.8%). These results were supported by Emmert *et al*.[15], who found that stroke rates were 2.3% in on-pump patients and 0.7% in off-pump patients. When compared to on-pump CABG, off-pump CABG generally shows a tendency toward fewer neurological problems, including stroke; nevertheless, the results should be interpreted cautiously because to heterogeneity and varied study designs.

Sá *et al*.[19] concluded that there was no indication of significant treatment effect heterogeneity in the stroke investigations. Random effect model: RR 0.793, 95% CI 0.660–0.920, *P=0.049*; total RR (95% CI) of stroke demonstrated a statistically significant difference in favor of off-pump CABG compared to on-pump CABG.

When compared to on-pump CABG, the individual OR primarily support off-pump CABG, suggesting a decreased risk of stroke. For example, Magee *et al*.[11] showed a substantial decrease with an OR of 0.07 (95% CI: 0.03, 0.20), while Abraham *et al*.[10] reported an OR of 0.32 (95% CI: 0.10, 1.05). The random-effects model's overall pooled OR is 0.43 (95% CI: 0.24, 0.76), indicating that off-pump CABG is linked to a 57% lower risk of stroke than on-pump CABG. This is supported by the common effect model, which has an OR of 0.48 (95% CI: 0.37, 0.62). Nonetheless, a significant degree of heterogeneity exists amongst the trials (I2=70%, *P<0.01*), suggesting that the outcomes vary. In spite of this variation, overall, off-pump CABG is obviously trending in the direction of lower stroke incidence, which suggests that it may be beneficial for improving neurological outcomes.

Van Dijk *et al*.[21], it is anticipated that 139 patients had random assignment to have on-pump surgery and 142 patients underwent off-pump surgery between March 1998 and August 2000. In the on-pump group, there were an average of 2.6 grafts per patient, whereas in the off-pump group, it was 2.4. In both patient groups, the mean time between surgery and the 5-year follow-up was 62 months (SD, 3 months) (*P=0.98*).

Given this, Sá *et al*.[19] calculated that their research adds value by showing that, in comparison to on-pump CABG, off-pump CABG lowers the risk of postoperative stroke. This data also demonstrates that there is no substantial reduction in the incidence of postoperative myocardial infarction and short-term all-cause mortality following off-pump CABG.

Age, sex, or the quantity of grafts performed do not seem to have any bearing on the prospective advantages of off-pump CABG on these outcomes. Off-pump CABG's impact on stroke has been a contentious issue; the majority of studies have found no benefit[22,23]. There was no trend or impact for a decrease in stroke in the two biggest studies to date, Lamy *et al*.[24] with 4752 patients and Shroyer *et al*.[25] with 2143 patients.

The on-off study, the most current study to be released, had 411 individuals and did not demonstrate any improvement in the incidence of stroke. No trial has been able to show significant differences between the groups regarding the outcome "stroke" to date, according to Afilalo *et al*.[26]. This is because more than 10 000 patients in a trial would be required to obtain a probabilistic sample and detect statistically significant differences regarding the outcome. Less aortic manipulation during off-pump CABG than during on-pump CABG may help to explain the decreased incidence of stroke. In order to minimize cerebral embolic events during off-pump CABG with clampless facilitating devices, El Zayat *et al*.[27] showed in an randomized controlled trial how crucial it is to prevent clamp, which proves that less manipulation of the aorta decreases the incidence of stroke.

Female and older patients are assumed to be more vulnerable to the dangers associated with on-pump CABG and, thus, to benefit more from off-pump CABG[28,29].

Significant variations exist in the frequency of transient ischemic episodes (TIA) between on-pump and off-pump CABG surgeries, according to studies by Naseri *et al*.[14] and Yokoyama *et al*.[9]. According to Naseri *et al*.[14], there is a significant decrease in the incidence of TIA after off-pump CABG, with 5% of off-pump patients experiencing TIA compared to 15.3% of on-pump patients. Additionally, Yokoyama *et al*.[9] reported that the off-pump group saw a reduction in neurological problems, such as TIA. According to these results, off-pump CABG may be a safer choice for lowering this particular neurological problem because it is linked to a considerably lower risk of TIA than the on-pump method.

In this particular situation, MACE was discovered in the best bypass surgery study comparing off-pump and on-pump CABG[30]. Lemma *et al*.[16] observed that in high-risk patients undergoing both on-pump and off-pump CABG, the frequency of postoperative neurologic problems was comparable in a randomized study. Wang *et al*.[20] discovered in a meta-analysis that in high-risk patients without substantial heterogeneity, the incidence rate of neurologic complications, including TIA, following off-pump CABG was 44% lower than that following on-pump CABG. This suggests that for patients with high surgical risk, off-pump CABG may be a safe and successful surgery.

Off-pump CABG lowers the need for blood transfusions and prevents the negative effects of CPB on the brain, kidney, and myocardium as compared to on-pump CABG. High-risk patients will gain a great deal from these off-pump CABG benefits. Indeed, a retrospective analysis has shown that in high-risk patients, off-pump CABG dramatically decreased the frequency of perioperative complications[31].

There is evidence that CPB may be harmful to the brain. Kilo *et al*.[32] used the P300 auditory-evoked potential to test cognitive brain function both before and after CABG. They discovered that the use of CPB was an independent predictor of reduced cognitive brain function following CABG. After CABG, systemic inflammatory response syndrome produced by CPB may have a role in the development of neurologic problems. Systemic inflammatory response syndrome was linked to an increased risk of stroke in individuals with ST-elevation myocardial infarction, according to research by van Diepen *et al*.[33].

Moreover, CPB necessitates aortic cannulation and may cause microthrombosis and nonpulsatile flow, which can lead to perioperative cerebral hypoperfusion and thromboembolism. Infarction may also result from plaques that break off from the aortic arch[21]. The aorta is preserved, and pulsatile flow is maintained with off-pump CABG. Consequently, off-pump CABG reduces the risk of aortic arch plaque falling off and allows for the maintenance of adequate perioperative cerebral perfusion[34]. Off-pump CABG can thereby lower the frequency of neurologic problems following surgery.

According to Cleveland *et al*.[35], implementing an off-pump technique in this situation also resulted in a reduction in the risk-adjusted complication rate, which went from 14.15% with on-pump CABG to 10.62% with OFCAB. In summary, there was a significantly lower risk of mortality and serious sequelae among patients who received OFCAB. To emphasize this further, a study found that patients receiving off-pump treatment experienced less complications (8.8% compared 14.0%) and death (2.7% against 4.0%)[36]. Thus, the previously cited data emphasize the significance of OFCAB in lowering mortality and morbidity as well as less postoperative problems.

Van Dijk *et al*.[21] also discovered that in terms of cardiovascular events at 5 years, there was an absolute difference of 3.1%; 95% confidence interval, − 6.1% to 12.4%; *P=0.55*; between 30 (21.1%) patients assigned to undergo off-pump surgery and 25 (18.0%) patients assigned to undergo on-pump surgery. Twenty-three (17.7%) patients in the off-pump group and 16 (12.3%) patients in the on-pump group had recurrent angina (absolute difference, 5.4%; 95% confidence range, −3.3 to 14.0%; *P=0.23*).

Naseri *et al*.[14] revealed an OR of 0.40 (95% CI: 0.10, 1.62), suggesting a decreased incidence of TIA in the off-pump group but one that was not statistically significant. An OR of 0.52 (95% CI: 0.19, 1.40) was discovered by Yokoyama *et al*.[9], which further suggests a decreased but not statistically significant TIA risk with off-pump CABG. In comparison to on-pump CABG, off-pump CABG may lower the risk of TIA by almost 53%, according to the random-effects model's overall pooled OR of 0.47 (95% CI: 0.21, 1.07). However, this conclusion is not statistically significant. With a low level of heterogeneity (I2=0% and *P=0.77*), the findings are similar between the trials. These results point to a tendency with off-pump CABG toward a decreased incidence of TIA, but further studies with larger sample sizes are needed to confirm this potential benefit.

Sisillo *et al*.[12], Marasco *et al*.[13], and Magee *et al*.[11] conducted research that shed light on neurological outcomes, including cognitive impairment, that occurs after CABG surgeries performed on-pump as opposed to off-pump. According to Sisillo *et al*.[12], stroke rates were 1.54% for on-pump patients and 1.34% for off-pump patients, respectively. Additionally, there was a somewhat lower incidence of cognitive impairment in off-pump patients (0.70%) than in on-pump patients (0.83%). Notwithstanding these results, there was no discernible variation in the overall neurological outcomes. Marasco *et al*.[13] examined general neurocognitive results from many trials totaling 892 participants. Magee *et al*.[11] centered on diabetic patients and presented data for 2545 on-pump and 346 off-pump cases, with the off-pump group exhibiting a much-reduced rate of cognitive impairment. Overall, the data point to a tendency toward somewhat reduced rates of cognitive damage following off-pump CABG; nevertheless, important variables like renal impairment and prior risk need to be taken into account when assessing neurological outcomes.

In this regard, several transcranial Doppler investigations have revealed that on-pump CABG patients had much greater rates of cerebral vascular embolization than off-pump CABG patients. According to Van Dijk *et al*.[37], the majority of studies that looked at neurocognitive function found that there was a slight decline in on-pump CABG patients' cognitive function compared to OFCAB patients in the short term (<2 to 3 months), but no discernible difference was found after a year. According to different research, off-pump CABG was associated with 160±19.5 cerebral microemboli, but on-pump CABG was connected to 575±278.5. This resulted in considerably lower cerebral perfusion to the left temporal lobe, bilateral occipital, precunei, thalami, and cerebellar regions postoperatively. Yet, it was shown that cerebral perfusion with off-pump CABG remained unaltered[38]. In light of this, off-pump CABG considerably lowers the risk of cerebral microemboli compared to those undergoing on-pump CABG surgery.

Sisillo *et al*.[12] found an OR of 0.85 (95% CI: 0.43, 1.66), suggesting that there was no discernible difference in the two groups' levels of cognitive impairment. According to Marasco *et al*.[13], off-pump CABG significantly reduced cognitive impairment [OR of 0.45 (95% CI: 0.31, 0.66)]. With an OR of 0.46 (95% CI: 0.28, 0.77), Magee *et al*.[11] also found a substantial decrease in cognitive impairment for off-pump treatments. The random-effects model's overall pooled OR is 0.51 (95% CI: 0.38, 0.67), indicating that, in comparison to on-pump CABG, off-pump CABG is linked to a roughly 49% lower risk of cognitive impairment. The low heterogeneity (I2=25%, $P=0.26$) suggests that the findings from the various investigations are consistent. When compared to the on-pump method, these results cumulatively point to a considerable advantage of off-pump CABG in lowering cognitive impairment.

Van Dijk *et al*.[21] found that, in this particular context, 62 (50.4%) of 123 patients in the off-pump group and 59 (50.4%) of 117 patients in the on-pump group had cognitive decline (absolute difference, 0%; 95% confidence interval, −12.7% to 12.6%; $P>0.99$) when applying the standard definition of cognitive decline (20% decline in 20% of the main test variables). Forty-one (33.3%) patients in the off-pump group and 41 (35.0%) patients in the on-pump group experienced cognitive deterioration, according to the alternative, more conservative criterion (absolute difference, −1.7%; 95% confidence range, −13.7% to 10.3%; $P=0.79$).

Three months following surgery, the Octopus Study revealed a trend toward improved cognitive results; however, this difference vanished at 12 months, and as of 5 years later, it still does not seem to exist. This is noteworthy because a number of studies[21,39,40] have shown that cerebral embolization is lower following off-pump CABG surgery than following on-pump CABG surgery.

Alternatively, the cognitive impairment that was noted at the 5-year follow-up might have been the result of aging naturally rather than the surgery[41].

There was insufficient evidence found in two trials comparing individuals following angioplasty to CABG surgery for postprocedural cognitive impairment. These trials undervalue the notion that, when it comes to the risk of developing cognitive decline, patient characteristics may matter more than the kind of intervention. It seems improbable that a genuine incidence of 50% cognitive deterioration occurs 5 years following surgery. There are several approaches to characterizing cognitive impairment. There seems to be some imprecision in the conventional definition (20% decline in performance in 20% of the variables) that was used. Despite reports of this definition's sensitivity and reliability, it was recently shown that the cutoff value may fall within the range of a person's normal performance fluctuations[42–44].

CONCLUSION

Based on our study results, it was estimated that off-pump CABG is associated with a lower incidence of neurological complications than on-pump CABG.

CONFLICT OF INTEREST

There are no conflicts of interest.

REFERENCES

1. Zhang RJZ, Yu XY, Wang J, Lv J, Yu MH, Wang L, Liu ZG. Comparison of in-hospital outcomes after coronary artery bypass graft surgery in elders and younger patients: a multicenter retrospective study. J Cardiothorac Surg 2023; 18:53.

2. Karabdic IH, Straus S, Granov N, Hadzimehmedagic A, Berberovic B, Kabil E, Kurtagic D. Off pump versus on pump coronary artery bypass grafting: short-term outcomes. Acta Inform Med 2023; 31:107.

3. Zhang S, Huang S, Tiemuerniyazi X, Song Y, Feng W. A meta-analysis of early, mid-term and long-term mortality of on-pump vs. off-pump in redo coronary artery bypass surgery. Front Cardiovasc Med 2022; 9: 869987.

4. Quin JA, Wagner TH, Hattler B, Carr BM, Collins J, Almassi GH, Shroyer AL. Ten-year outcomes of off-pump vs on-pump coronary artery bypass grafting in the Department of Veterans Affairs: a randomized clinical trial. JAMA Surg 2022; 157:303–310.

5. Ali MG, Siam TF, Fouda TE, Elnaggar AM. Incidence of postoperative neurological complications after off-pump versus on-pump coronary artery bypass surgery in the early postoperative period. Execut Editor 2020; 11: 167.

6. Dominici C, Salsano A, Nenna A, Spadaccio C, El-Dean Z, Bashir M, *et al*. Neurological outcomes after on-pump vs off-pump CABG in patients with cerebrovascular disease. J Card Surg 2020a; 34: 941–947.

7. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986; 7: 177–188.

8. Tufanaru C, Munn Z, Stephenson M, Aromataris E. Fixed or random effects meta-analysis? Common methodological issues in systematic reviews of effectiveness. JBI Evid Implement 2015; 13:196–207.

9. Yokoyama T, Baumgartner FJ, Gheissari A, Capouya ER, Panagiotides GP, Declusin RJ. Off-pump versus on-pump coronary bypass in high-risk subgroups; 2000. Available at: http://www.sts.org/section/atsdiscussion/

10. Abraham R, Karamanoukian HL, Jajkowski MR, von Fricken K, D'Ancona G, Bergsland J, Salerno TA. Does avoidance of cardiopulmonary bypass decrease the incidence of stroke in diabetics undergoing coronary surgery? Heart Surg Forum 2001; 4: 135–140.

11. Magee MJ, Dewey TM, Acuff T, Edgerton JR, Hebeler JF, Prince SL, Mack MJ. Influence of diabetes on mortality and morbidity: off-pump coronary artery bypass grafting versus coronary artery bypass grafting with cardiopulmonary bypass; 2001. Available at: http://www.ctsnet.org/doc/4314

12. Sisillo E, Marino MR, Juliano G, Beverini C, Salvi L, Alamanni F. Comparison of on pump and off pump coronary surgery: risk factors for neurological outcome. Eur J Cardiothorac Surg 2007; 31: 1076–1080.

13. Marasco SF, Sharwood LN, Abramson MJ. No improvement in neurocognitive outcomes after off-pump versus on-pump coronary revascularisation: a meta-analysis. Eur J Cardio-thorac Surg 2008; 33: 961–970.

14. Naseri MH, Pishgou B, Ameli J, Babaei E, Taghipour HR, Mohammad C, Naseri H. Comparison of post-operative neurological complications between on-pump and off-pump coronary artery bypass surgery. Pak J Med Sci 2009; 25:1.

15. 15. Emmert MY, Salzberg SP, Seifert B, Rodriguez H, Plass A, Hoerstrup SP, Falk V. Is off-pump superior to conventional coronary artery bypass grafting in diabetic patients with multivessel disease?. Eur J Cardiothorac Surg 2011; 40: 233–239.

16. Lemma MG, Coscioni E, Tritto FP, Centofanti P, Fondacone C, Salica A, Genoni M. On-pump versus off-pump coronary artery bypass surgery in high-risk patients: operative results of a prospective randomized trial (on-off study): J Thorac Cardiovasc Surg 2012; 143: 625–631.

17. Ji Q, Mei Y, Wang X, Ding W. On-pump versus off-pump coronary artery bypass surgery in high-risk patients a retrospective propensity score matching analysis. Int Heart J 2014; 55: 484–488.

18. Guerra N. On pump vs. off-pump surgery: still no definitive answers. Portug J Cardiac Thorac Vasc Surg 2022; 29: 9–11.

19. Sá MP, Ferraz PE, Escobar RR, Martins WN, Lustosa PC, Nunes EDO, Lima RC. Off-pump versus on-pump coronary artery bypass surgery: meta-analysis and meta-regression of 13,524 patients from randomized trials. Braz J Cardiovasc Surg 2012; 27:631–641.

20. Wang J, Gu C, Gao M, Yu W, Li H, Zhang F, Yu Y. Comparison of the incidence of postoperative neurologic complications after on-pump versus off-pump coronary artery bypass grafting in high-risk patients: a meta-analysis of 11 studies. Int J Cardiol 2015; 185:195-197.

21. van Dijk D, Spoor M, Hijman R, Nathoe HM, Borst C, Jansen EW, Octopus Study Group. Cognitive and cardiac outcomes 5 years after off-pump vs on-pump coronary artery bypass graft surgery. JAMA 2007; 297:701–708.

22. Feng ZZ, Shi J, Zhao XW, Xu ZF. Meta-analysis of on-pump and off-pump coronary arterial revascularization. Ann Thorac Surg 2009; 87: 757–765.

23. Wijeysundera DN, Beattie WS, Djaiani G, Rao V, Borger MA, Karkouti K, Cusimano RJ. Off-pump coronary artery surgery for reducing mortality and morbidity: meta-analysis of randomized and observational studies. J Am Coll Cardiol 2005; 46: 872-882.

24. Lamy A, Devereaux PJ, Prabhakaran D, Taggart DP, Hu S, Paolasso E, Yusuf S. Off-pump or on-pump coronary-artery bypass grafting at 30 days. New Engl J Med 2012; 366: 1489–1497.

25. Shroyer AL, Grover FL, Hattler B, Collins JF, McDonald GO, Kozora E, Novitzky D. On-pump versus off-pump coronary-artery bypass surgery. New Engl J Med 2009; 361: 1827–1837.

26. Afilalo J, Rasti M, Ohayon SM, Shimony A, Eisenberg MJ. Off-pump vs. on-pump coronary artery bypass surgery: an updated meta-analysis and meta-regression of randomized trials. Eur Heart J 2012; 33: 1257–1267.

27. El Zayat H, Puskas JD, Hwang S, Thourani VH, Lattouf OM, Kilgo P, Halkos ME. Avoiding the clamp during off-pump coronary artery bypass reduces cerebral embolic events: results of a prospective randomized trial. Interact Cardiovasc Thorac Surg 2012; 14: 12–16.

28. Lima R, Diniz R, Césio A, Vasconcelos F, Gesteira M, Menezes A, Escobar M. Myocardial revascularization in octogenarian patients: retrospective and comparative study between patients operated on pump and off pump. Braz J Cardiovasc Surg 2005; 20:8–13.

29. Sá MP, Lima LP, Rueda FGD, Escobar RRD, Cavalcanti PEF, Escobar MASD, Lima RDC. Comparative study between on-pump and off-pump coronary artery bypass graft in women. Braz J Cardiovasc Surg 2010; 25:238–244.

30. Møller CH, Perko MJ, Lund JT, Andersen LW, Kelbæk H, Madsen JK, Steinbrüchel DA. No major differences in 30-day outcomes in high-risk patients randomized to off-pump versus on-pump coronary bypass surgery: the best bypass surgery trial. Circulation 2010; 121:498–504.

31. Al-Ruzzeh S, Nakamura K, Athanasiou T, Modine T, George S, Yacoub M, Amrani M. Does off-pump coronary artery bypass (OPCAB) surgery improve the outcome in high-risk patients?: a comparative study of 1398 high-risk patients. Eur J Cardiothorac Surg 2003; 23: 50–55.

32. Kilo J, Czerny M, Gorlitzer M, Zimpfer D, Baumer H, Wolner E, Grimm M. Cardiopulmonary bypass affects cognitive brain function after coronary artery bypass grafting. Ann Thorac Surg 2001; 72: 1926–1932.

33. van Diepen S, Vavalle JP, Newby LK, Clare R, Pieper KS, Ezekowitz JA, Granger CB. The systemic inflammatory response syndrome in patients with ST-segment elevation myocardial infarction. Crit Care Med 2013; 41: 2080–2087.

34. Zamvar V, Williams D, Hall J, Payne N, Cann C, Young K, Dunne J. Assessment of neurocognitive impairment after off-pump and on-pump techniques for coronary artery bypass graft surgery: prospective randomised controlled trial. BMJ 2002; 325: 1268.

35. Cleveland Jr JC, Shroyer ALW, Chen AY, Peterson E, Grover FL. Off-pump coronary artery bypass grafting decreases risk-adjusted mortality and morbidity. Ann Thorac Surg 2001; 72: 1282–1289.

36. Plomondon ME, Cleveland Jr JC, Ludwig ST, Grunwald GK, Kiefe CI, Grover FL, Shroyer AL. Off-pump coronary artery bypass is associated with improved risk-adjusted outcomes. Ann Thorac Surg 2001; 72: 114–119.

37. Van Dijk D, Jansen EW, Hijman R, Nierich AP, Diephuis JC, Moons KG, Octopus Study Group. Cognitive outcome after off-pump and on-pump coronary artery bypass graft surgery: a randomized trial. JAMA 2002; 287: 1405–1412.

38. Knipp SC, Matatko N, Wilhelm H, Schlamann M, Massoudy P, Forsting M, Jakob H. Evaluation of brain injury after coronary artery bypass grafting. A prospective study using neuropsychological assessment and diffusion-weighted magnetic resonance imaging. Eur J Cardiothorac Surg 2004; 25: 791–800.

39. Keizer AMA, Hijman R, Kalkman CJ, Kahn RS, Van Dijk D, Octopus Study Group). The incidence of cognitive decline after (not) undergoing coronary artery bypass grafting: the impact of a controlled definition. Acta Anaesthesiol Scand 2005; 49: 1232–1235.

40. Ascione R, Ghosh A, Reeves BC, Arnold J, Potts M, Shah A, Angelini GD. Retinal and cerebral microembolization during coronary artery bypass surgery: a randomized, controlled trial. Circulation 2005; 112: 3833–3838.

41. Blauw GJ, Bollen ELEM, Van Buchem MA, Westendorp RGJ. Dementia at old age: a clinical end-point of atherosclerotic disease. Eur Heart J Suppl 2001; 3(suppl_ N): 16–19.

42. Selnes OA, Pham L, Zeger S, McKhann GM. Defining cognitive change after CABG: decline versus normal variability. Ann Thorac Surg 2006; 82: 388–390.

43. Hlatky MA, Bacon C, Boothroyd D, Mahanna E, Reves JG, Newman MF, Blumenthal JA. Cognitive function 5 years after randomization to coronary angioplasty or coronary artery bypass graft surgery. Circulation 1997; 96(9 Suppl): II–11.

44. Wahrborg P, Booth JE, Clayton T, Nugara F, Pepper J, Weintraub WS, Stables RH. Neuropsychological outcome after percutaneous coronary intervention or coronary artery bypass grafting: results from the Stent or Surgery (SoS) Trial. Circulation 2004; 110: 3411–3417.