Heliyon 9 (2023) e19735

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Effect of different coronary artery revascularization procedures on cognition: A systematic review

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ARTICLE INFO

Keywords:
Coronary revascularization
Cognitive domains
Coronary artery disease
Minimal invasive procedure

ABSTRACT

Coronary revascularization interventions have been associated with post-intervention cognitive decline. Hence, this systematic review aims to compare the long-term effects of different coronary revascularization interventions on cognition. The Cochrane Library and MEDLINE databases were searched for articles published between January 2009 and January 2023. Articles on clinical trials and cohort studies that compared at least two different interventions with a minimum three months follow up were included to evaluate the consequences of different intervention techniques on cognition. Each selected study was evaluated using a revised tool to assess the risk of bias in randomized trials (RoB 2), and Risk of Bias In Non-Randomized Studies - of Interventions (ROBINS-1) was used for evaluating non-randomized studies. Five eligible studies, with four different comparisons, were included. Out of these studies, three RCTs and two cohort studies were included A participants gone through different procedures; on-pump and off-pump coronary artery bypass grafting (CABG), Percutaneous coronary intervention (PCI conventional cardiopulmonary bypass (CCPB), the miniaturized cardiopulmonary bypass (MCPB) and endoscopic coronary artery bypass grafting (Endo-CABG). These comparisons showed that different interventions have different effects on cognition; however, there is no solid evidence of correlations between them. Thus, the results of this review suggest that there should be greater focus on comparing interventions and that a reasonable follow-up duration should be set to avoid the influence of confounders. There is also a need to determine the effect of long-term cognitive decline while reducing interference by other variables.

1. Introduction

"Cognition" is an inclusive term that encompasses the high-order neural processes that transfer and reinforce the handling of information generated by diverse neurological, psychological, and emotional factors [1]. Cognitive ability is defined as an extensive mental capability including reasoning, problem solving, planning, abstract thinking, complex idea comprehension, and learning from experience [2]. One approach classifies the domains by the general process involved; clear examples are memory, attention, planning, reasoning, language, and executive function [3]. A deficit or impairment can affect any of these functional domains and result in a cognitive disorder, which is defined as any disorder that seriously damages the cognitive functions of the individual to the level where normal functioning, whether it be a basic function or a complex function in society, is impossible without treatment intervention [4].

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https://doi.org/10.1016/j.heliyon.2023.e19735
Received 15 May 2023; Received in revised form 28 August 2023; Accepted 31 August 2023
Available online 1 September 2023

Cognitive deficits are not wholly associated with specific diseases and may be symptoms or indications of an underlying condition. A cognitive deficit and the associated cognitive disorder may be temporary or permanent [4].

Coronary artery disease (CAD) has been found to correlate with cognitive deficit and dementia [5,6]. A recent systematic review reported an association between a remarkable increase in the coronary calcium score and the incidence of dementia [7]. Moreover, a correlation between cardiac medications and the risk of dementia has been reported in multiple systematic reviews and meta-analyses [8–10]. Revascularization interventions used for CAD management have also been found to correlate with cognitive impairment. Percutaneous coronary intervention (PCI), a minimally invasive procedure, and coronary artery bypass grafting (CABG), a major surgical procedure, have been found to improve myocardial ischemia, quality of life, cardiac function, and cardiac-related mortality rates [11–13]; however, they have also been found to correlate with the incidence of cognitive impairment following intervention [14]. A possible reason for this is the formation of cerebral emboli during the intervention [15,16]. In PCI, there are two possible mechanisms for emboli formation: emboli originating during the manipulation of the atheromatous wall of the aortic arch or emboli originating from air bubbles introduced by coronary catheters [15]. In CABG, emboli form when a cardiopulmonary bypass device is used. Therefore, employing the off-pump technique (i.e., not using a cardiopulmonary bypass device) decreases the occurrence of cerebral emboli [17].

In one study, the incidence of short-term postoperative cognitive impairment (i.e., within a few weeks post-intervention) in individuals after CABG was found to be 20–50% [18]. In another recent systematic review, the rate of short-term postsurgical cognitive impairment among post-CABG patients was reported to be more than 40% at hospital discharge [19]. The findings of Kennedy et al. (2013) suggested that using a cardiopulmonary bypass approach during CABG is not necessarily associated with cognitive reduction, with no significant difference between the use of on- and off-pump approaches [20]. Moreover, McGinn et al. (2009) compared the long-term cognitive outcome of three groups of cardiac patients who either underwent on- or off-pump CABG or who did not need the surgery [21] found that baseline factors, such as age and level of education, affected the long-term cognitive outcome significantly more than the type of intervention used.

Advances in surgical techniques have led to the development of minimally invasive cardiac procedures that have proven to be feasible and have positive short-term outcomes, such as reductions in hospitalization rates, mortality rates, recovery time, and the occurrence of wound infection [22–24]. For example, minimally invasive direct coronary artery bypass is an off-pump technique performed using a small left thoracotomy without a sternotomy [25]. Another example is endoscopic coronary artery bypass grafting (Endo-CABG), which is primarily based on the classic CABG procedure but uses a thoracoscopic technique instead of a median sternotomy. This innovative procedure is used to treat patients with multivessel CAD. Several positive outcomes have been reported for this procedure, including reductions in postoperative pain and hospitalization time and rapid recovery and return to work [23,24]. One observational cohort study compared postoperative cognitive impairment in two groups that underwent Endo-CABG or PCI [26]. No differences were found between the groups within three months post-procedure. The only notable findings were that patients in the Endo-CABG group exhibited the greatest reductions in "processing speed" and "verbal memory" and that patients in the PCI group showed the greatest reductions in "processing speed," followed by "working memory" and "attention." One explanation is that retrograde arterial perfusion, used during these minimally invasive procedures, might correlate with an increased incidence of neurological complications, followed by an increased risk of cerebral embolic complications [27].

Several studies have been conducted on the effects of different coronary artery intervention approaches on different domains of cognitive function [21,28,29]. In one study, cognitive decline was compared among patients who had undergone either CABG, thoracic surgery, or no surgery (control group). The CABG group had lower results than other surgical group pre-operatively, and improvement was observed in this group for up to eight weeks post-intervention [29]. Almost all of the patients in the CABG group returned to their pre-operative cognitive function status, and 25% improved to such an extent that they exceeded their pre-operative baseline function. Another group of researchers measured outcomes over a longer period of follow-up in three groups: patients with CAD who underwent CABG, patients with CAD who received non-surgical (medical) treatment, and healthy participants [21]. The results showed that both the CABG and non-surgical groups had a significant late decline in different cognitive domains between 12 and 72 months post-intervention compared to the healthy participant group.

A limited number of systematic reviews have investigated the effects of different treatment approaches on cognition and have compared these approaches to identify any variation in cognitive outcome [14,19,20,30]. A recent systematic review compared cognitive outcomes between participants who underwent CABG or PCI [14], and another review compared the outcomes of on- and off-pump CABG [20]. However, to date, no review has investigated the effect of different cardiac interventions (e.g., PCI, on-pump CABG, off-pump CABG, and minimally invasive cardiac procedures) on cognitive function. For this reason, the aim of this systematic review was to compare the long-term post-intervention cognitive function in patients who underwent different coronary artery revascularization interventions. We anticipate that the findings of this review will be useful during decision-making about the choice of treatment course and will provide a better understanding of the correlation between long-term cognitive decline and different coronary revascularization interventions.

The research question that has been addressed by this review is as follows: How do different coronary artery revascularization interventions affect cognition in patients with coronary artery disease?

P: Patients who underwent a coronary intervention (e.g., CABG, PCI, or minimally invasive CABG).

I: Coronary artery revascularization intervention.

C:Another coronary artery revascularization intervention (e.g., CABG, PCI, or minimally invasive CABG).

O: Cognitive function.

2. Methods

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [31]. This protocol is registered in the PROSPERO (International prospective register of systematic reviews) database with ID: CRD42022375334.

2.1. Search strategy

The MEDLINE and Cochrane Library databases were searched for articles published between January 2009 and January 2023. This period was selected because of the remarkable development in surgical and interventional procedures and the increase in the number of older individuals who underwent cardiac interventions that occurred during this time [14]. The Medical Subject Headings (MeSH) search terms utilized were: ("Coronary Artery Bypass") OR ("Percutaneous Coronary Intervention/adverse effects" OR "Percutaneous Coronary Intervention/psychology") OR ("Myocardial Revascularization/adverse effects" OR "Myocardial Revascularization/-psychology") OR ("Angioplasty, Balloon, Coronary/adverse effects" OR "Angioplasty, Balloon, Coronary/psychology") AND ("Cognition" OR "Cognition Disorders" OR "Mental Status and Dementia Tests") OR ("Neuropsychological Tests"). The results were limited to published, full-text articles that were peer-reviewed, written in English, and involved humans.

The resultant articles were screened by two independent reviewers. Also, the reference lists of the full-text articles were checked for additional articles to include. Conflicts and disputes were resolved by general agreement within the research team.

2.2. Study eligibility

Articles on clinical trials and cohort studies that compared at least two different interventions were included to evaluate the consequences of different intervention techniques on cognition. Moreover, to be included in the systematic review, articles were required to report a cognitive outcome measured using a neuropsychological test battery with sufficiently high sensitivity to detect early cognitive impairments and to provide more data about the specific domains included [32]. Also, only studies with at least a three-month follow-up period were included.

Review articles, qualitative studies, case series, case reports, and low-quality studies were excluded. Book chapters, protocol papers, reviews, conference abstracts, and articles with incomplete reporting of the chosen outcomes were excluded. Finally, duplicate articles and studies were also excluded.

2.3. Quality assessment

Each selected study was evaluated using a revised tool to assess the risk of bias in randomized trials (RoB 2) [33], and Risk of Bias In Non-Randomized Studies - of Interventions(ROBINS-1) [34] was used for evaluating non-randomized studies. In all non-experimental studies, the risk of bias due to confounding was appraised as moderate. Patients cannot be blinded in randomized trials as they undergo procedures; however, we concluded that this factor would not influence the outcome.

2.4. Data extraction

Data on the following parameters were extracted from the selected studies: sample size, participants' age and gender, cognitive decline evaluation criteria, and the pre- and post-intervention measured values for each criterion. All measurement data were collected from the immediate post-intervention time point to the final follow-up time point. The follow-up period of each study depended on the duration of each study.

2.5. Data analysis

It was not appropriate to perform a quantitative analysis due to the small number of articles to be analyzed and the heterogeneity of the outcome measurements within the articles. However, a systematic review of the studies' findings was conducted by comparing the outcomes that correlated with the use of PCI, different CABG techniques, and minimally invasive coronary artery bypass.

To analyze cognitive deficit, multiple analyses were conducted using data obtained from different time points (pre-intervention baseline, immediate post-intervention, post-intervention, and final measurement). Multiple time points were selected to evaluate the outcomes instead of a single time point to capture any variation in cognitive impairment over time and thus generate more accurate results in terms of long-term effects.

3. Results

The flow chart in Fig. 1 shows the process used to select articles for this review. Initially, the search identified 4640 articles from two databases. Then, 4391 were excluded after the titles and abstracts were reviewed. A further 244 studies were excluded during the full article accurate assessment stage for different reasons, such as data being reported in other articles [35], the article being written in a language other than English [36], irrelevant comparison being presented [37,38], or even an inappropriate time frame was used [39,40]. When the article selection process was completed, five eligible studies remained [21,26,30,41,42]. All the included studies are

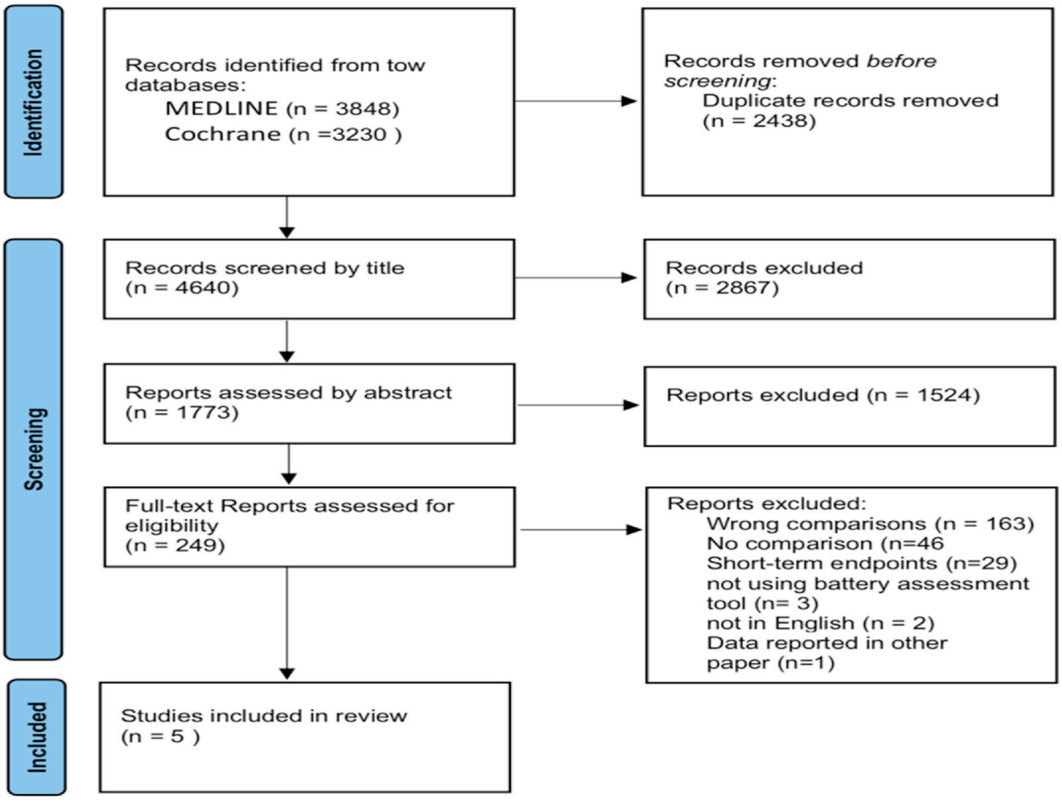

Fig. 1. PRISMA flow diagram.

listed in Table 1, while their demographic data are available in Table 2. Out of five studies, three RCTs and two cohort studies were included whith participants gone through different procedures; on-pump and off-pump CABG, PCI, conventional cardiopulmonary bypass (CCPB), the miniaturized cardiopulmonary bypass (MCPB) and Endo-CABG. Some included studies had more than two groups, but for the purpose of this review, we included only the intervention groups and excluded all others, such as medically treated and healthy participants [21,26]. In one article, the study groups were based on whether the participants underwent cognitive assessment or not; only data related to those who underwent the cognitive assessment were included in this review [30].

The results of the risk bias assessment performed on the selected articles are summarized in Table 3 for the randomized control trials and in Table 4 for the cohort studies. The included studies ranged between low risk [26,41,42] to some concerns/moderate risk [21,30].

The cognitive domains in which the participants' performance was studied as an outcome differed among the articles, as shown in Table 5. The domains to be included were generally determined by the test battery used in each study. The most commonly tested domains were attention and different types of memory.

3.1. Comparison between PCI and CABG

Only one experimental study compared the outcomes of PCI and off-pump CABG [30]. The off-pump CABG group had fewer cognitive deficits during the 7.5-year follow-up (combined Z-score of 0.11 for off-pump CABG vs. 0.17 for PCI; difference = 0.28, 95% confidence interval [CI] = 0.08–0.47, $p < 0.01$). This statistically significant result was diminished after applying a multivariable linear regression model. The results of the off-pump CABG group were better than those of the PCI group in three domains: learning (Mean 0.15 standard deviation SD [0.04] vs. PCI -0.18 [1.48], $p = 0.03$), motor capacity (0.16 [0.91] vs. PCI -0.17 [1.69], $p = 0.03$), and verbal memory (0.17 [0.90] vs. PCI -0.19 [1.07], $p = 0.01$). In this study, no cognitive evaluation was conducted at the baseline time point, which means that it is not possible to compare the results between or within the groups. The baseline characteristics were similar between the two groups, except impaired left ventricular function was more common in the off-pump CABG (22%) compared to that in the PCI group (11%).

3.2. Comparison between off-pump CABG and on-pump CABG

The outcomes in patients who underwent off-pump CABG were compared to those in patients who underwent on-pump CABG to identify the effect of using a cardiopulmonary bypass machine during CABG. Two articles were found that compared these outcomes: a

Table 1
Summary of included study in the systematic review.

Authors	Type	N	Intervention	Control	Follow-up	Outcome measures	Inclusion criteria	Exclusion criteria	Results
Kozora et al., 2010 [42]	RCT single-blind	2203	on-pump CABG	Off-pump CABG	1 year	neuropsychological test battery	elective or stable urgent CABG-only (from the protocol of the ROOBY trial [43]).	1. CABG combined with valve surgery. 2. Emergency, hemodynamically unstable patients, or received cardiogenic shock before the surgery. 3. Moderate to severe valve disorder. 4. Subjects enrolled in different experimental research. 5. Documented history of major diffuse disease in distal vessels or of small target coronary arteries. 6. Any reservations about certain patient that the clinical care team have including in the study with a well-explained documentation. 7. Subjects with a history of being un-adhere to follow-up appointments. 8. Subject-stated preference for particular treatment arm. 9. Inability to provide informed consent. (from the protocol of the ROOBY trial [43].	at 1 year, both groups had decline. 12.0% of the on-pump and 13.2% of the off-pump (p = 0.595).
Selnes et al.. 2009 [21]	Cohort study	395	on-pump CABG	Off-pump CABG	6 years	neuropsychological test battery	Patients who can perform neuropsycological evaluation, able to a documented consent, English native speaker, not on mechanical ventilator.	No exclusion was done for medical reasons.	No difference between the groups in most of cognitive domains except the off-pump group showed less decline in visual memory (P = 0.03) and vasoconstriction (P = 0.02).
Sauër et al.2013 [30]	RCT	280 But 201 with cogniti-ve tests	PCI	Off-pump CABG	7.5 years	neuropsychological test battery	Patients with angina (stable or unstable), documented ischemia and both off-pump or PCI were regarded technically feasible.	Patients with LM- stenosis, total occlusion artery, akinetic myocardial area, interventions required more than 1 graft of LCX, impaired ventricular function, urgent procedures, Q-wave infarct within the last 6 weeks, history of angioplasty within 6 months, history of CABG, coagulation disorders or intolerance to acetylsalicydic acid or ticlopidine.	Off-pump CABG vs. PCI: Z-Score difference 0.28 with off-pump CABG has better cognitive results. After linear regression difference 0.14 (statistical significance is lost).
Yuhe et al., 2022[41]	single-blinded RCT	78	MCPB	CCPB	3 months	neuropsychological test battery	Age between 21 and 85 years without a cardiac surgical history before.	poor LVEF (<30%), immunity disorders or malignancies, acute inflammatory disease, coagulation disorders, steroid treatment, massive carotid disorder, and on dialysis.	Rate of cognitive decline at the endpoint; CCPB 51.4%, MCPB 50.0%, P = 0.90. No significant difference.
Stessel et al., 2020[26]	cohort study	138	Endo-CABG	PCI	3 months	neuropsychological test battery	Non but the control group included healthy age and sex-matched subjects to the intervention group.	a history of postsurgical cognitive deterioration, delirium or stroke, symptomatic CAD, dementia, renal or hepatic dysfunction, a formal history of abusing drug or alcohol and presence of physical conditions or a language barrier that cause inability to perform the neurological evaluation.	Endo-CABG: n = 6 [13.0%]; PCI: n = 7 [15.9%], p = 0.732. No significant differences between the groups.

N= Number of participants; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting surgery; LM-stenosis = left main stenosis; CCPB= Conventional cardiopulmonary bypass; MCPB = Miniaturized cardiopulmonary bypass, LVEF = left ventricle ejection fraction; CAD = coronary artery disease.

Table 2
Baseline demographics in the included studies with comparison between different intervention and control groups.
CABG = coronary artery bypass grafting surgery; PCI = percutaneous coronary intervention; CCPB= Conventional cardiopulmonary bypass; MCPB = Miniaturized cardiopulmonary bypass.

	Group	Kozora et al., 2010(42)	Selnes et al.. 2009 [21]	Sauër et al.2013 [30]	Yuhe et al., 2022 [41]	Stessel et al., 2020[26]
Age, y (mean ± SD)	control	On-pump 61.7	On-pump 63.6	PCI 59	CCPB 61.0	PCI 64,65
	intervention	Off-pump 62.2	Off-pump 66.0	Off-pump 57	MCPB 59.8	EndoCABG 64,61
Sex (male), %	control	On-pump 99.3	On-pump 76	PCI 70	CCPB 74.3	PCI 84,09
	intervention	Off-pump 99.5	Off-pump 72	Off-pump 77	MCPB 69.4	EndoCABG 82,61
Diabetes, %	control	On-pump 44.1	On-pump 30	PCI 9	CCPB 45.7	PCI 4,54
	intervention	Off-pump 39.1	Off-pump 37	Off-pump 14	MCPB 58.3	EndoCABG 26,08
Hypertension, %	control	On-pump 85.0	On-pump 64	PCI 32	CCPB 80	PCI 68.18
	intervention	Off-pump 84.0	Off-pump 68	Off-pump 43	MCPB 91.7	EndoCABG 54,35
Previous stroke, %	control	On-pump 7.6	On-pump 5	PCI 5	CCPB coagulopathy was exclusion criteria	PCI stroke was exclusion criteria
	intervention	Off-pump 7.1	Off-pump 3	Off-pump 5	MCPB coagulopathy was exclusion criteria	EndoCABG stroke was exclusion criteria
Education, y	control	On-pump Not reported	On-pump 14.1	PCI 4.1	CCPB Not reported	PCI Not reported
	intervention	Off-pump Not reported	Off-pump 13.4	Off-pump 4.3	MCPB Not reported	EndoCABG Not reported

Table 3
Risk of Bias assessment for randomized controlled trial(ROB2).

	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Kozora et al., 2010[42]	low	low	high	Low	low	Low
Sauër et al., 2013 [30]	Low	Some concerns	Some concerns	Some concerns	Low	Some Concerns
Yuhe et al., 2022[41]	Low	Low	Low	Low	Low	Low

Table 4
Risk of Bias assessment for cohort studies(ROBINS-1).

	Pre-intervention		At intervention	Post-intervention				
	Bias due to confounding	Selection Bias	Classification Bias	deviations from intended interventions	missing data	Bias due to measurement of outcomes	Reporting Bias	Overall
Selnes et al., 2009 [21]	Low	Low	Low	Unclear	Low	Low	Low	Moderate
Stessel et al., 2020[26]	Moderate	Low	Low	Low	Low	Low	Low	Low

Table 5
Cognitive measurements of included studies.

Study	Cognitive domains
Kozora et al., 2010 [42]	Immediate and delayed recall for verbal and nonverbal material, immediate auditory attention and visuomotor speed, motor speed, visuospatial and graphomotor processes.
Selnes et al. 2009 [21]	Verbal memory, Visual memory, Visuoconstruction, Language, Motor speed, and Psychomotor speed, Attention, Executive function, Global.
Sauër et al.2013 [30]	Verbal memory, Motor capacity, Divided attention, Reaction time, Decision making, and Working memory, Learning.
Yuhe et al., 2022 [41]	Immediate memory, delayed memory, attention, visuospatial ability, and language.
Stessel et al., 2020 [26]	Verbal memory, Attention, processing speed, Working memory, and Motor function.

randomized control study [41] and a prospective cohort study [21]. In the randomized control study, Kozora et al. (2010) [42] included elective or stable urgent CABG cases only and excluded others based on the criteria listed in Table 2. In the prospective cohort study, Selnes et al. (2009) [21] only included patients who could participate in the neuropsychological evaluations, who were able to provide documented consent, and who were native English speakers; they did not exclude patients for any medical reasons. Regarding the follow-up period, Kozora et al. implemented a one-year endpoint, while Selnes et al. implemented a six-year follow-up, with neuropsychological assessments conducted before surgery (baseline) and 3, 12, 36, and 72 months after surgery.

Kozora et al. (2010) [42] found that 12.0% of the on-pump participants and 13.2% of the off-pump participants ($p = 0.595$) had reduced cognitive function one year post-intervention. Conversely, cognitive improvement (determined as ≥ 1 SD on two or more tests) was observed in 37.9% of the on-pump participants and 41.6% of the off-pump participants ($p = 0.207$). Also, the off-pump participants demonstrated greater improvement in their Clock Drawing Test results than the other participants ($p = 0.003$) at the one-year time point. Nevertheless, most of the cognitive assessment results were within the normal range at the baseline and one-year time points. A difference in the endpoint results between the two groups was seen only in two tests. In terms of logical memory delayed recall, 4.1% of the on-pump participants and 3.5% of the off-pump participants showed a decline from the normal pre-operative baseline to the endpoint, while 9.8% of the on-pump participants and 15% of the off-pump participants showed improvement (from diminished to normal) during the follow-up period ($p = 0.02$).

In their longitudinal study, Selnes et al. (2009) reported two types of results [21]. First, they determined whether there was any difference between the pre-operative (baseline) and the 72-month follow-up measurements. They found that there were no consistent differences among the intervention groups regarding cognitive alteration over time. The off-pump participants showed smaller changes than the on-pump participants in two domains: visual memory (mean 0.20 SD[-0.02, 0.41], p = 0.03) and visuoconstruction (0.01 [−0.15, 0.16], p = 0.02). However, there were no significant variations in the other domains and the global score. Second, they determined whether there were any changes in the measurements between the 12- and 72-month time points. The on-pump participants had a higher degree of late cognitive impairment in multiple domains, with a significant reduction in verbal memory ($p = 0.04$), visuoconstruction ($p = 0.01$), language ($p = 0.03$), executive function ($p = 0.01$), and the global composite domain ($p = 0.01$). Generally, the cognitive changes that occurred between the 12- and 72-month time points were greater than those that occurred during the longer follow-up period, from the pre-operative time point to the 72-month time point.

3.3. Comparison between CCPB and MCPB

A recent study by Yuhe et al. (2020) compared two cardiopulmonary bypass techniques used during on-pump CABG and had a three-month follow-up period [41]. The authors found that there was no significant difference in the occurrence of cognitive decline among patients in the conventional cardiopulmonary bypass (CCPB) group and the miniaturized cardiopulmonary bypass (MCPB) group ($P = 0.90$). They also investigated whether certain risk factors correlated with postoperative cognitive impairment and found that having less than six years of formal education independently correlated with postoperative cognitive decline in participants in the CCPB group (relative risk, RR = 3.014, CI = 1.054–8.618, $P = 0.040$). Also, the lowest hematocrit levels recorded during the cardiopulmonary bypass procedure independently correlated with postsurgical cognitive impairment among the participants in the MCPB group (RR = 0.931, CI = 0.868–0.998, $P = 0.044$).

3.4. Comparison between PCI and Endo-CABG

The final comparison examined in this review was conducted by Stessel et al. (2020) and was between PCI (a non-surgical intervention) and Endo-CABG (a minimally invasive surgical technique) [26]. The difference in the incidence of postoperative cognitive decline was not significant between the two groups after three months of follow-up (Endo-CABG = 13.0% vs. PCI = 15.9%, p = 0.732). Regarding the effect on specific cognitive domains, participants who underwent Endo-CABG showed the greatest impairment in their “processing speed” (Trail Making Test B [20.5%] and WAIS-III Digit Symbol Coding Test [19.6%]) and “verbal memory” (Rey Auditory Verbal Learning Test Delayed Recall Score [16.6%]). Participants who underwent PCI showed a greater reduction in their “processing speed” (Trail Making Test B [34.5%]), followed by “working memory” (WAIS-III Digit Span Forward [21.4%]) and “attention” (Trail Making Test A [18.0%]).

4. Discussion

The findings of this systematic review show the long-term effects that different coronary revascularization techniques have reportedly had on different cognitive domains. A search for articles on this topic revealed that only five relevant studies have been conducted; most of the published articles screened in this review were found to compare patients who underwent surgical intervention with medically treated patients or healthy participants. The results of such comparisons are only useful when determining whether a specific surgical intervention is superior to a medical treatment or not. However, as we know, medication is not suitable or sufficient in some cases, and surgical intervention is required. Hence, there is a need for more comparative research that examines different types of interventions to identify the outcomes, including the impact on cognition.

The impacts of PCI and CABG on cognitive impairment were compared in one study [30]. The results showed that there were no significant differences between the studied groups during the 7.5-year follow-up, especially after performing a multivariable linear regression to eliminate the effect of confounders. As the authors mentioned, the study’s results were as expected due to a lack of baseline cognitive assessment results being collected before the intervention. Moreover, the study included patients of all ages, even elderly patients, and had a prolonged follow-up period, which emphasized the effect of aging (a main predictor) on cognitive impairment [44,45]. Other limitations of this study include the small sample size, the sampling technique used (which may indicate selection bias), and the fact that neither a normality test nor regression analysis was performed.

The second study we examined compared the outcomes of two CABG techniques: off- and on-pump CABG. Kozora et al. (2010) found no convincing clinical evidence of cognitive impairment one year after intervention [42]. Multiple variables might have influenced their results, including that only 54.3% of the participants had complete cognitive datasets recorded in the follow-up period. Moreover, these participants were younger and had better cognitive baseline function than the participants who did not continue until the end of the study. The actual age mean of those who completed the study was not mentioned, but the fact that their cognitive baseline values were normal or semi-normal contrasts with the evidence that shows that CAD, besides cardiovascular disorders, is a risk factor for cognitive decline. Regarding the analysis, the sample size was smaller than that calculated with a power of 80%, which affected the power of the study, and no normality test was used. Therefore, given the gaps in the data and the limitations of the analysis, the results cannot be generalized to the population, despite the large sample size.

Selnes et al. (2009) [21] compared the outcomes of the same CABG techniques examined by Kozora et al. over a longer period. They found that there were more favorable outcomes associated with off-pump CABG than on-pump CABG, regardless of whether values recorded pre-intervention or 12 months after intervention were compared to those recorded 72 months after intervention. They also found that certain domains were the most or least impaired over time. To our knowledge, no similar study has been conducted with such a prolonged follow-up period; therefore, it is challenging to compare the findings of this study with any others. However, the findings of one study conducted with a three-month endpoint agree with these results [46]. It is worth noting that these results contrast with the findings of a large systematic review and meta-analysis [20], which suggested that undergoing a cardiopulmonary bypass may not correlate with cognitive decline. Moreover, the long follow-up period may have increased the influence of confounding factors, such as age, education level, baseline cognitive function, and diabetes [45]. Finally, the fact that no patients were excluded for any medical reason means that any psychosocial changes that the patients experienced during the 72 months of follow-up may have affected the results.

The third comparison we examined was between the new MCPB (minimally invasive extracorporeal circulation) procedure and the CCPB procedure. Yuhe et al. [41] found no significant difference in cognitive impairment between patients who underwent MCPB and those who underwent CCPB. They did, however, find correlations with other factors. This is the first study that compared these strategies in terms of their impact on cognition. A large systematic review found that patients who underwent MCPB demonstrated a reduced incidence of stroke compared to those who underwent CCPB, with no difference in neurological events [47]. A commentary about the safety and variability of MCPB configurations emphasized that MCPB may be more beneficial for infants with congenital cardiac disease [48].

The last addressed comparison is between PCI and Endo-CABG. Stessel et al. [26] found that there was no significant difference in cognitive domain decline three months after intervention between patients who underwent PCI and patients who underwent Endo-CABG. The authors did not explain whether there were any differences in the patients' baseline characteristics or provide a P value. They referred to the positive neurological outcome as a result of the shorter duration of the cardiopulmonary bypass procedure. The mean occlusion time during Endo-CABG is only about 50 min at the center where the study was conducted, which may affect the results. The study by Yuhe et al. compared Endo-CABG and conventional open CABG across different outcome measures [41]. The results showed the superiority of Endo-CABG in terms of the length of stay in the ICU and hospital, cost effectiveness, and number of transfusions. This comparison is more logical as they compared two CABG categories, while Stessel et al. (2020) compared PCI and minimal CABG [26]. In most cases, CABG is performed after PCI fails, which makes it a more invasive strategy requiring longer duration and perfusion. The authors may have intended to show that the Endo-CABG technique has a positive outcome in terms of cognition and when compared to PCI.

The heterogeneity of the outcome measurements in the included studies can be seen in multiple aspects starting with type of the studies and the given interventions. The main disparity among the included studies were differences in the end-points that ranged between three months [26,41] to 7.5 years [30]. Also, each study has different inclusion and exclusion criteria in addition to the cognitive domains being tested.

We used RoB 2 and ROBINS-1 for the assesmsnt of risk bias in randomized and nonrandomized studies respectively. In all of the five included studies, blinding to the type of procedure was not possible; however, we believe that this factor did not affect their performance. Kozora et al. (2010)'s study had a high attrition rate, which led to a high risk of bias due to missing outcome data [42]. Also, Sauër et al. (2013) did not report the cognitive assessment results at baseline [30]. In the included cohort studies, Selnes [21] et al. (2009) and Stessel [26] et al. (2020) only reported the cardiovascular risk factors of the cardiac participants and not those of the healthy participants. However, the bias due to confounding in Selnes et al. (2009)'s study received a low score because the cardiac intervention groups were the target of this review, and our comparisons excluded the healthy or medically treated groups [21,26]. The bias due to confounding in Stessel et al.(2020)'s study received a moderate score because they only reported the NYHA score for the Endo-CABG and not for the PCI group [26]. The quality influence the validity of the study results as studies with high risk of bias or poor methodology tend to exaggerate the effect and may lead to incorrect inferences.

This review has multiple limitations, including that a small number of studies were included and that the search strategy only covered two databases and articles written in English. The search strategy was also limited to articles published between January 2009 and January 2023, following the strategy used in another review [14]. Restricting the search to this period may have resulted in the exclusion of some relevant articles; however, the aim was to minimize the variation among the included studies in areas such as the surgical or anesthesia techniques used, medication development, and changes in the population undergoing surgery [14]. Furthermore, only including studies that used battery tests and not other types of cognitive assessment tests (e.g., questionnaires) is a limitation of this study. This decision was made because battery cognitive tests generate more valid, accurate, and holistic results than other types of tests [49].

It has also highlighted that there is a dearth of studies in this area and a clear need for future research to focus on comparing the outcomes of different surgical interventions, rather than on comparing the outcomes of individual surgical interventions with those of medical treatments or in healthy participants. Such studies will provide insight into the real effects and outcomes of different interventions. We also recommend setting a reasonable time limit for performing follow-up measurements to avoid the strong influence of multiple confounders, such as aging, on long-term results. Our final recommendation is to standardize the neuropsychological tests used and cognitive domains studied to minimize diversity among studies.

5. Conclusion

In conclusion, different interventions have different effects on cognition; however, there is currently not a sufficient body of strong evidence to confirm reported correlations. Finally, it is critical to determine the effect of coronary revascularization interventions on long-term cognitive decline while reducing the influence of other contributing factors.

APC waived - waiver code: Heliyon - Contractual payment discounts.

[item-group:IG000074].

Source of funding

This research did not receive any specific grant from funding agencies in public, commercial, or not-for-profit sectors.

Author contribution statement

All authors listed have significantly contributed to the development and the writing of this article.

Data availability statement

Data will be made available on request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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