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REVIEW

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Risk factors of delirium after cardiac surgery: a systematic review and meta-analysis

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Abstract

Background Post-operative delirium (POD) is a relatively common occurrence following surgical procedures, particularly cardiac surgeries. Given that the majority of pharmacologic treatments for delirium have demonstrated inadequate efficacy, it is of great importance to identify risk factors to prevent delirium or reduce its complications. Consequently, in this systematic review and meta-analysis, we identified risk factors of POD after cardiac surgery.

Method A comprehensive search of the literature was conducted using the databases Scopus, PubMed, and Web of Science from the inception to April 22, 2024. The objective was to identify prospective cohorts that had assessed the risk factors associated with POD in patients undergoing cardiac surgery using multivariate regression.

Results Of the 3,166 studies that were initially screened, 23 were included in the review. Nine risk factors were evaluated including age (OR 1.06, 95% CI (1.04, 1.08), $p<0.001$), pre-operative depression (OR 3.71, 95% CI (2.45, 5.62), $p<0.001$), post-operative atrial fibrillation (AF) (OR 2.39, 95% CI (1.79, 3.21), $p<0.001$), hypertension (HTN) (OR 1.64, 95% CI (0.75, 3.56), $p=0.212$), age ≥ 65 (OR 3.32, 95% CI (2.40, 4.60), $p<0.001$), pre-operative AF (OR 4.43, 95% CI (2.56, 7.69), $p<0.001$), diabetes mellitus (OR 2.16, 95% CI (1.39, 3.35), $p=0.001$), combined coronary artery bypass graft (CABG) + valve surgery (OR 2.73, 95% CI (1.66, 4.49), $p<0.001$), and cardiopulmonary bypass (CPB) time (OR 1.02, 95% CI (1.01, 1.04), $p=0.001$).

Conclusions A total of nine risk factors were evaluated, from which eight were found to have a statistically significant effect on the risk of developing POD. These factors can be employed to more effectively identify at-risk patients and to prevent the occurrence of POD. Furthermore, this approach can facilitate earlier diagnosis and more effective patient care.

Keywords Delirium, Cardiac surgery, Risk factors, Meta-analysis

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Introduction

The incidence of post-operative delirium has been reported to be high following both cardiac [1, 2] and non-cardiac surgeries [3, 4]. A meta-analysis of 91 studies revealed that the incidence of POD after cardiac surgery (32%) was higher than that after orthopedic (20%), vascular (14%), spinal (13%), colorectal (14%), abdominal (30%), urologic (10%), and mixed surgeries (26%) [5]. The incidence of POD after cardiac surgery has been reported to vary considerably across different studies, ranging from 2.8 to 63.8% [6–28].

To date, the majority of pharmacologic treatments for delirium have demonstrated inadequate efficacy, and most interventions are focused on identifying risk factors and preventing delirium or managing symptoms and reducing complications [29–36]. A number of risk factors have been identified for POD in patients who have undergone cardiac surgery. These include advanced age, depression, postoperative atrial fibrillation, hypertension, diabetes mellitus, history of stroke, length of operation, ICU stay or mechanical ventilation, and other factors [6–28]. Nevertheless, the impact of these factors on POD remains a topic of ongoing debate [6–28]. Furthermore, given the aforementioned reasons, the identification of risk factors that contribute to the development of delirium is of significant importance for the prevention and early intervention of POD. Consequently, conducting a comprehensive and accurate systematic review and meta-analysis is essential for elucidating the relationship between these risk factors and POD, which is crucial for effective POD management.

Previously, several systematic reviews have evaluated the risk factors of POD after cardiac surgery [22, 37–40]. However, these reviews are either out of date or did a narrow search with few keywords, which resulted in the omission of some eligible studies. This study represents a comprehensive and updated systematic review and meta-analysis, focusing exclusively on risk factors extracted from multivariate analysis performed in cohort studies. Furthermore, we extracted risk factors irrespective of whether they were identified as significant or insignificant in the original study. Our objective was to determine which risk factors are independently associated with POD after cardiac surgery and to contribute to more effective management of POD by preventing and controlling those factors.

Method

Search strategy

A comprehensive search was conducted in Scopus, PubMed, and Web of Science from the inception to April 22, 2024. To mitigate the risk of overlooking pertinent studies, we employed a comprehensive set of keywords, encompassing the following search terms:

("risk factor" OR "risk factors" OR (factor AND risk) OR "Social Risk Factors" OR (Factor AND "Social Risk") OR (Factors AND "Social Risk") OR ("Risk Factor" AND Social) OR ("Risk Factors" AND Social) OR "Social Risk Factor" OR "Health Correlates" OR (Correlates AND Health) OR "Population at Risk" OR "Populations at Risk" OR "Risk Scores" OR "Risk Score" OR (Score AND Risk) OR "Risk Factor Scores" OR "Risk Factor Score" OR (Score AND "Risk Factor") AND ("cardiac surgery" OR (Surgery AND Heart) OR (Surgery AND Cardiac) OR "Heart Surgery" OR "coronary artery bypass grafting" OR "cardiopulmonary bypass" OR "open heart" OR CABG OR "coronary artery surgery" OR "valve surgery" OR "coronary artery bypass surgery") AND (delirium OR "subacute delirium" OR (delirium AND subacute) OR (deliriums AND subacute) OR "subacute deliriums" OR "delirium of mixed origin" OR "mixed origin delirium" OR "mixed origin deliriums" OR "delirious" OR "confusion" OR "acute confusional state" OR "acute confusional syndrome"). Subsequently, we created syntaxes tailored to each database using the aforementioned keywords, which are available in Additional file 3. In addition, the first five pages of Google Scholar were also examined. Following the retrieval of the studies, the Endnote 8 reference manager software was employed to identify and remove duplicates. Once the screening and selection process was complete, we conducted a thorough examination of the reference lists of the included studies and previously published reviews to identify any potential missing. The study protocol for this article was registered in PROSPERO (CRD42024538371). Furthermore, all the terms of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline were adhered to.

Inclusion and exclusion criteria

The inclusion criteria for this study were as follows: 1) The study should be a prospective cohort study evaluating risk factors for post-operative delirium in adult patients (>18 years old) undergoing cardiac surgery.

2) Delirium should be assessed using either the fourth or fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV or DSM-V), the Confusion Assessment Method (CAM), the Confusion Assessment Method for the ICU (CAM-ICU), or the Intensive Care Delirium Screening Checklist (ICDSC). 3) The study should employ multivariate regression analysis to analyze the identified risk factors. 4) The study results should be reported as an odds ratio (OR) with a 95% confidence interval (CI), or this information could be extracted from the available data in the study.

The exclusion criteria were as follows: (1) Studies conducted on patients undergoing transcatheter procedures. (2) Non-English studies.

Data extraction and outcome measures

The studies retrieved through the search strategy were transferred to EndNote for the purpose of removing duplicates. The remaining studies were then subjected to a screening process based on their titles and abstracts, with the objective of identifying those that were likely to meet the eligibility criteria. This was carried out by two authors independently. Subsequently, two authors independently assessed the full texts of the remaining studies for eligibility, and those that met the criteria were identified. Any discrepancies were resolved through discussion. Two independent reviewers then extracted the following data from the selected studies using a pre-designed form: the first author's name, the year of publication, the country in which the study was conducted, the sample size, the number of patients in the exposure and comparison groups, the mean age, the percentage of males, the type of cardiac surgery, the method used to assess delirium, and the risk factors with their corresponding OR and 95% CI. Any discrepancies in here were also resolved through discussion.

A risk factor was deemed eligible for inclusion in the study if its OR and 95% CI were reported in at least three of the included studies in a multivariate regression analysis. The determination of significance or non-significance did not influence our decision-making process regarding risk factors.

Risk of bias assessment

The risk of bias for each included study was independently assessed by two authors using the Newcastle-Ottawa Scale (NOS) tool [41]. Cohort studies were evaluated based on their selection (4 stars), comparability (2 stars), and outcome (3 stars). Any discrepancies between the two authors were resolved through consensus. The overall quality of the studies was evaluated and classified as either "good", "fair", or "poor". A study was considered to have a high quality if its overall score was at least seven, and if the sections in which it lacked quality were not of the same category. A study was considered to have poor quality if it received a score of 0 or 1 in each of the aforementioned categories. In the absence of any of the aforementioned circumstances, the quality of the study was deemed to be fair.

Data synthesis and statistical analysis

The study aimed to identify risk factors for post-operative delirium. If a risk factor was reported by three or more studies using multivariate regression, its effect sizes were pooled using the "metan" command in Stata version 14.0 (StataCorp, TX, USA). The pooled effect size utilized in this study was the OR and its 95% CI. The statistical heterogeneity between the studies was evaluated using the Cochrane chi-square test and the I^2 statistics. Heterogeneity was considered to be present if the p-value was less than 0.1 or the I^2 value was greater than 50%. In the event of heterogeneity, a random-effects model was employed. Otherwise, a fixed-effects model was used.

Subgroup analysis

A subgroup analysis was conducted for meta-analyses comprising more than five studies. The analysis was conducted based on mean age, male percentage, and sample size for all risk factors, as well as based on study quality and delirium assessment tool for two risk factors. This was done in order to identify the sources of heterogeneity and the major factors affecting post-operative delirium.

Sensitivity analysis

To ascertain the robustness of our findings, a sensitivity analysis was conducted using the one-out remove method for one of the risk factors. This analysis aimed to determine whether the exclusion of a single study could significantly impact the results.

Publication bias

In order to detect any potential publication bias, both a funnel plot and Egger's test were employed. First, we constructed funnel plots for each meta-analysis comprising at least five studies. Based on the symmetry or asymmetry of these plots, we employed Egger's test to supplement our findings.

Results

Search results and study characteristics

The total number of studies retrieved in our primary search was 2407 from Scopus, 1189 from Web of Science, and 971 from PubMed. Following the removal of duplicates, 3,166 studies entered the screening phase. The relevance and desired design of the studies were then evaluated based on their titles and abstracts, and 131 studies were considered for selection process. Finally, 67 articles were excluded because they did not report the outcome of interest. Additionally, 13 articles were excluded because they had not used a valid tool to assess delirium, 13 articles were excluded because they were non-English studies, 5 articles were excluded because they were duplicate publications, 4 articles were excluded because they included non-cardiac surgery patients, 2 articles were excluded because they included transcatheter procedures, 1 article was excluded because it did not conduct multivariate regression, 1 article was excluded because it included pediatric patients, 1 article was excluded because it was not a prospective cohort, and 1 article was excluded because it was conducted on the same population as another study, which had a larger sample size. The number of studies meeting our eligibility criteria was 23 [6–28]. The methodology employed in the selection of these articles is illustrated in a flowchart (Fig. 1).

The characteristics of the included studies are presented in Table 1. A total of 14,847 patients were included in the study, with 1,751 in the delirium group and 13,098 in the non-delirium group. The incidence of POD was observed to range from 2.8 to 63.8%. Fifteen studies were conducted on patients undergoing CABG and/or valve surgery. One study limited its patients to those undergoing valve surgery, while others included various open heart surgeries. The Cam-ICU method for assessing delirium was employed in sixteen studies, six studies utilized the DSM-IV criteria, and one employed the ICDSC tool. Nine studies evaluated the effect of each year increase in age as a risk factor for POD, seven studies evaluated pre-operative depression, six studies evaluated post-operative AF, five studies evaluated HTN, four studies evaluated age≥65, and three studies evaluated each of the following: presence of diabetes mellitus, pre-operative AF, each minute increase in CPB time, and the effect of combined CABG+valve surgery on POD as a risk factor (Table 1).

Risk of bias

The NOS tool was employed for the evaluation of risk of bias (ROB) in the included studies. The results are presented in the Additional file 4. Overall, the quality of the studies was deemed to be good in 17 studies and fair in six studies. Not a single study included in this analysis was of poor quality.

The results of systematic review and meta-analysis

We evaluated 9 risk factors for the development of POD following cardiac surgery. A total of nine studies investigated the impact of an increase in age on the risk of POD. Eight studies reported a significant increase in risk, while one study reported an insignificant increase. The overall effect of each year of age increase on the risk of POD after cardiac surgery was significant (OR 1.06, 95% CI (1.04, 1.08), $p<0.001$, I2: 57.4%) (Additional file 2). Of the seven studies investigating the presence of pre-operative depression, six reported a significant increase in the risk of developing POD after cardiac surgery, while one reported an insignificant increase. After pooling data from the aforementioned studies, it was found that the presence of pre-operative depression significantly increased the risk of post-operative delirium (OR 3.71, 95% CI (2.45, 5.62), $p<0.001$, I2: 12.7%) in patients

Table 1 The characteristics of included studies

Study Included	Year of Publication	Sample Size	Incidence of Delirium	Delirium Assessment Tool	Extracted Risk Factors	Reference
Cheng	2021	152	6.57%	CAM-ICU	Pre-operative depression	[6]
Jung	2015	133	18.04%	CAM-ICU, CAM	Pre-operative depression	[7]
Katznelson	2009	**1059**	11.52%	CAM-ICU	Pre-operative depression, CABG+valve surgery	[8]
Kazmierski	2014	113	36.28%	CAM-ICU	Pre-operative depression, post-operative AF	[9]
Kazmierski	2010	**563**	16.34%	DSM-IV	Pre-operative depression, pre-operative AF, age≥65	[10]
Kazmierski	2006	260	11.53%	DSM-IV	Pre-operative depression, pre-operative AF, age≥65	[11]
Krzych	2013	**5781**	4.08%	DSM-IV	Hypertension, age≥65	[12]
Kupiec	2020	149	20.13%	CAM-ICU	Pre-operative depression, CPB time	[13]
Li	2022	379	**63.85%**	CAM-ICU	Age	[14]
Mariscalco	2012	**3154**	2.82%	CAM-ICU	Age, hypertension, post-operative AF, CABG+valve surgery	[15]
Mu	2010	243	**50.61%**	CAM-ICU	Age, diabetes mellitus	[16]
Nguyen	2023	285	19.64%	CAM-ICU	Age, post-operative AF, CPB time	[17]
Ogawa	2018	313	14.69%	ICDSC	Age	[18]
Oliveira	2018	173	34.1%	DSM-IV	Hypertension, post-operative AF	[19]
Osse	2012	125	46.4%	CAM-ICU	CABG+valve surgery	[20]
Santos	2004	220	33.63%	DSM-IV	Age, hypertension, post-operative AF	[21]
Smulter	2013	142	**54.92%**	DSM-IV	Age, diabetes mellitus	[22]
Vahdat	2019	296	22.97%	CAM-ICU	Age	[23]
Velayati	2020	398	17.08%	CAM-ICU	Hypertension	[24]
Wang	2020	186	15.59%	CAM-ICU	Age	[25]
Wang	2023	232	12.06%	CAM-ICU	CPB time	[26]
Zhang	2022	242	29.75%	CAM-ICU	Diabetes mellitus, post-operative AF, age≥65	[27]
Zhang	2015	249	30.52%	CAM-ICU	pre-operative AF	[28]

CABG: coronary artery bypass graft surgery, AF: atrial fibrillation, CPB: cardiopulmonary bypass undergoing cardiac surgery (Additional file 2). Additionally, all six studies evaluating the occurrence of post-operative AF found a significant relationship between the two (OR 2.39, 95% CI (1.79, 3.21), $p<0.001$, I2: 0.0%) (Additional file 2). Four studies indicated a higher risk of developing POD in patients with HTN, while one study revealed that HTN has a strong protective effect against developing POD after cardiac surgery. However, upon pooling the data, the effect of hypertension on postoperative delirium following cardiac surgery did not reach statistical significance (OR 1.64, 95% CI (0.75, 3.56), $p=0.212$, I2: 84.9%) (Additional file 2). All four studies investigating age≥65 as a risk factor found that post-operative delirium was more probable to occur in the elderly after cardiac surgery (OR 3.32, 95% CI (2.40, 4.60), $p<0.001$, I2: 0.0%) (Additional file 2). Studies evaluating the impact of pre-operative AF, diabetes mellitus, and combined CABG and valve surgery found that POD was more prevalent among patients with pre-operative AF, diabetes mellitus, and who underwent combined surgery (OR 4.43, 95% CI (2.56, 7.69), $p<0.001$, I^2: 0.0%), (OR 2.16, 95% CI (1.39, 3.35), $p=0.001$, I^2: 0.0%), (OR 2.73, 95% CI (1.66, 4.49), $p<0.001$, I^2: 50.6%), respectively) (Additional file 2). Additionally, the findings indicated that each additional minute of CPB time was associated with a minimal but positive and statistically significant increase in the probability of developing POD following cardiac surgery (OR 1.02, 95% CI (1.01, 1.04), $p=0.001$, I2: 57.2%) (Additional file 2).

Subgroup analysis

A series of subgroup analyses were conducted to evaluate the impact of each year increase in age, pre-operative depression, and post-operative AF as a risk factor for POD following cardiac surgery (Additional file 5).

Age

The results of subgroup analyses demonstrated that the risk of developing POD for each year increase in age was not significantly different between studies with mean age of equal to or greater than 65 years (OR 1.04, 95% CI (1.02, 1.07), I^2: 19.6%) and less than 65 years (OR 1.05, 95% CI (1.04, 1.07), I^2: 72.4%), between studies in which the male percentage of patients was equal to or greater than 65% (OR 1.04, 95% CI (1.03, 1.06), I^2: 70.4%) versus when it was less than 65% (OR 1.07, 95% CI (1.04, 1.09), I^2: 33.8%), or when the study quality was good (OR 1.04, 95% CI (1.03, 1.06), I^2: 53.4%) versus fair (OR 1.07, 95% CI (1.04, 1.09), I^2: 59.4%) (Additional file 5). However, when stratified by sample size, studies in which sample size was less than 250 (OR 1.11, 95% CI (1.07, 1.14), I^2: 0.0%) exhibited a greater risk of developing POD for each additional year of age compared to studies with a sample size of greater than 250 (OR 1.04, 95% CI (1.02, 1.05), I^2: 9.8%) (Additional file 5).

Pre-operative depression

After conducting subgroup analyses, it was observed that in the presence of pre-operative depression, there was no difference in the risk of developing POD between studies with mean age of equal to or more than 64 years (OR 2.96, 95% CI (1.50, 5.87), I^2: 60.0%), versus less than 64 years (OR 5.33, 95% CI (2.69, 10.56), I^2: 0.0%) (Additional file 5). The same pattern was observed for studies in which the proportion of male patients was equal to or greater than 72% (OR 2.78, 95% CI (1.31, 5.92), I^2: 60.2%), in comparison to studies where the proportion of male patients was less than 72% (OR 4.21, 95% CI (2.56, 6.91), I^2: 0.0%), the studies with a sample size of greater than 250 patients (OR 3.96, 95% CI (2.24, 7.00), I^2: 0.0%) versus studies with a sample size of less than 250 patients (OR 3.45, 95% CI (1.88, 6.33), I^2: 49.1%), and when the delirium assessment tool used was the CAM-ICU (OR 3.30, 95% CI (2.03, 5.37), I^2: 32.8%) versus when it was the DSM-IV (OR 5.08, 95% CI (2.29, 11.28), I^2: 0.0%) (Additional file 5).

Post-operative AF

After conducting subgroup analyses, it was found that there was no difference in the risk of developing POD in patients with post-operative AF between studies with a mean age of equal to or greater than 65 years (OR 2.11, 95% CI (1.48, 3.01), I^2: 0.0%) in comparison to studies with a mean age of less than 65 years (OR 2.85, 95% CI (1.39, 5.84), I^2: 16.9%), when the male population comprised at least 70% of the study population (OR 2.01, 95% CI (1.29, 3.13), I^2: 47.9%), compared to studies where the male population comprised less than 70% of the study population (OR 2.52, 95% CI (1.59, 3.98), I^2: 0.0%), in studies with a sample size of >250 (OR 2.02, 95% CI (1.37, 2.98), I^2: 0.0%), versus studies with a sample size of <250 (OR 2.76, 95% CI (1.59, 4.81), I^2: 0.0%), in studies with a good methodological quality (OR 2.67, 95% CI (1.60, 4.46), I^2: 0.0%), versus studies with a fair methodological quality (OR 2.27, 95% CI (1.59, 3.25), I^2: 0.0%), and in studies where the CAM-ICU tool was used for assessing delirium (OR 2.34, 95% CI (1.67, 3.30), I^2: 12.0%), vs. when the DSM-IV tool was used (OR 2.54, 95% CI (1.43, 4.51), I^2: 0.0%) (Additional file 5).

Sensitivity analysis

To assess the robustness of our results, we conducted a sensitivity analysis for the effect of each year increase in age as a risk factor for developing POD after cardiac surgery using the one-out remove method. Our findings indicated that excluding individual studies had little effect on the overall outcome and the results were not dependent on any individual study (CI: 1.03, 1.09) (Additional file 6).

Publication bias

We investigated publication bias for studies evaluating the impact of each year increase in age, the presence of pre-operative depression, and the occurrence of post-operative AF as risk factors for developing POD after cardiac surgery. The funnel plot demonstrated some asymmetry for all risk factors. The Egger's test indicated that the risk of publication bias for each year increase ($p=0.081$) and pre-operative depression ($p=0.08$) was not statistically significant. However, there was a strong suspicion that the results pertaining to post-operative AF where potentially influenced by publication bias ($p=0.018$). It is therefore recommended that the effects of post-operative AF as a risk factor be investigated in a study with a larger sample size.

Discussion

In this study, we aimed to identify the risk factors for the developing POD after cardiac surgery. We used only multivariate data and included risk factors regardless of whether they were significant or insignificant in the original study. Our review included 23 prospective cohort studies with 14,847 patients (Additional file 1). We evaluated 9 risk factors for the development of POD after cardiac surgery (Additional file 2). The reason we have found fewer risk factors compared with other systematic reviews is that other reviews have also included risk factors from univariate regression or included different types of study design, which may affect the reliability of the results [37–40]. Our results exhibited that each additional year of age increased the risk of developing POD following cardiac surgery, highlighting the need to perform elective cardiac surgery as soon as possible (Additional file 2). The presence of pre-operative depression and the occurrence of post-operative AF also increased the risk of POD (Additional file 2). Other risk factors for POD identified in our study include: older age (≥65 years), pre-operative AF, diabetes mellitus, undergoing combined CABG+valve surgery, and each additional minute of CPB time (Additional file 2). The risk factors identified for POD after cardiac surgery vary between studies. This is partly due to differences in populations and surgical protocols in different regions. Three of the most commonly reported risk factors for POD after cardiac surgery are age [22, 37, 38, 40], diabetes [22, 38, 40], and pre-operative depression [38–40], which is consistent with our findings. The results of the study conducted by Chen et al. [40] were comparable to our findings with regard to the three aforementioned risk factors. However, the authors did not identify certain risk factors that we had identified due to not including of some recent studies in their review and their narrow focus on risk factors resulting from elective surgery [40]. Conversely, our analysis did not identify some of the risk factors identified in that review as risk factors for POD, as our analysis did not include risk factors resulting from univariate analysis [40]. Keeping aside the three aforementioned risk factors and AF, which were also identified in the meta-analysis conducted by Lin et al. [38], that yielded somewhat different results. This discrepancy can be attributed to the fact that the study in question is relatively dated, encompasses only on-pump surgery, and includes both retrospective and prospective cohorts in addition to randomized controlled trials [38]. We will now proceed to a further discussion of the mechanisms involved in these three risk factors, which serve to increase the risk of POD. With regard to the aging process, the mechanisms involved in the reduction of the brain's functional reserve, including reductions in neural connections, synapses, and cerebral blood flow of the brain, or alterations such as protein overload, micro-infarcts or micro-bleedings or disruption of the blood-brain barrier, are thought to contribute to the susceptibility of the elderly to the development of delirium [42]. In the context of diabetes, there is evidence that diabetes can induce inflammation, neuropathy, and injury to the blood-brain barrier [43, 44]. For depression, there is evidence that it can render patients susceptible to delirium through alterations in monoamine neurotransmission, stress and inflammatory responses, elevated cortisol levels, and disrupted circadian rhythm [45, 46]. In contrast to aging, predisposing risk factors such as depression and diabetes can be prevented or better controlled in cardiac patients, making the role of studies such as ours in identifying such risk factors even more important.

In our subgroup analysis, we found that although age≥65 was a risk factor for POD, the relation between each additional year of age and the risk of developing POD was not different between the group with a mean age of equal to or more than 65 years and the younger group (Additional file 5). This suggests that the mechanisms associated with a higher prevalence of POD in older patients are distinct from those related to aging. Furthermore, subgroup analyses demonstrated that the mean age and gender distribution had minimal to no impact on the influence of each additional year of age, pre-operative depression, and post-operative depression on the incidence of POD (Additional file 5).

However, the relationship between the presence of HTN and the development of POD following cardiac surgery was not statistically significant (Additional file 2). This finding is consistent with the results of the meta-analysis by Chen, et al. [40]. This may be attributed to the opposite findings observed in the study conducted by Krzych, et al., [12], which comprised a considerably large population. Consequently, future studies with a larger sample size will be better able to evaluate this aspect.

This study has several notable strengths. Firstly, we used a comprehensive search strategy was employed, utilizing a multitude of related keywords, in order to minimize the risk of overlooking eligible studies. Second, we limited our inclusion criteria to prospective cohorts in order to draw robust conclusions based on homogeneous and robust studies. Third, the included studies were of high quality, thereby enhancing the reliability of our findings. Fourth, in contrast to previous studies, no data produced by univariate regression were extracted. Fifth, we also pooled effect sizes of all eligible risk factors that had been extracted from multivariate regression, despite the fact that the relation of some of them to the development of POD had been reported to be insignificant.

It should be noted that this review is also subject to certain limitations. First, we limited our review to prospective cohorts, a decision we believe was necessary but which may have resulted in the loss of some valuable data. Second, risk factors were included only if they were evaluated in at least three studies using multivariate. This represents a potential limitation, as the use of multiple regression is necessary to ascertain with certainty whether the observed effect for each risk factor is attributable to confounding factors. Consequently, the identification of a risk factor as an independent risk factor for POD is largely dependent on the authors' subjective decision regarding which factors to include in the multiple regression analysis. In conclusion, the question of whether risk factors such as length of ICU stay, mechanical ventilation, type of anesthetics used, frailty, and emergency surgery, which were mentioned as risk factors in many studies, are independent risk factors for the development of POD remains unanswered. It is hoped that future studies will further investigate the effects of these risk factors using multivariate regression. Third, there is a strong suspicion that the findings regarding post-operative AF may be influenced by publication bias. Therefore, it is recommended that this outcome be evaluated with a larger sample size. Fourth, there was a high degree of statistical heterogeneity observed among some of our outcomes including: age, combined CABG+valve surgery, HTN, and CPB time. However, through the implementation of multiple subgroup analyses, the source of heterogeneity for these outcomes was identified. Fifth, the diagnostic tools utilized to identify outcomes such as pre-operative depression, pre-operative delirium, pre-operative diabetes exhibited variability across different studies.

Conclusions

In this systematic review and meta-analysis, we identified 8 risk factors for the development of POD after cardiac surgery. Such information can assist clinicians in more effectively identifying patients at risk of delirium and in implementing strategies prevent it. It can also facilitate earlier diagnosis of delirium, which in turn allows for more appropriate care and a reduction in complications. For instance, the results of this study may prompt a closer attention to older patients with diabetes and a history of depression and atrial AF when performing CABG and valve surgery. Nevertheless, it is our hope that future studies will further investigate the effects of additional risk factors on the development of POD using multivariate regression.

Abbreviations

POD	Post-operative delirium
AF	Atrial fibrillation
HTN	Hypertension
CPB	Cardiopulmonary bypass
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
DSM	Diagnostic and Statistical Manual of Mental Disorders
CAM	Confusion Assessment Method
ICDSC	Intensive Care Delirium Screening Checklist
OR	Odds ratio
CI	Confidence interval
NOS	Newcastle-Ottawa scale
CABG	Coronary artery bypass graft
ROB	Risk of bias

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13019-024-03156-1.

Supplementary Material 1: search strategy

Supplementary Material 2: risk of bias assessment using Newcastle-Ottawa scale

Supplementary Material 3: funnel plot

Supplementary Material 4: sensitivity analysis

Supplementary Material 5: subgroup analysis

Supplementary Material 6: main analysis

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None.

Author contributions

BW conceptualized this article, performed the literature search, data extraction, and data analysis, and critically edited the article. YW performed the literature search and data extraction and wrote the draft.

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Data availability

Upon reasonable request, the corresponding author will provide data.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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