

The effect of depth of anesthesia monitoring on postoperative delirium: A narrative review

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Abstract

Background and Objective: Postoperative delirium (POD) is a common complication of surgery, associated with significant morbidity and additional health care costs. Postoperative cognitive dysfunction (POCD) overlaps with postoperative delirium, but is considered to occur in the months following hospital discharge. The primary aim of this narrative review was to assess the effect of the use of depth of anesthesia (DoA) monitoring on the incidence of postoperative delirium. Secondary aims were to examine the effect of using DoA monitoring on postoperative cognitive dysfunction and the total dosage of anesthetics used.

Methods: An extensive search of PubMed and Embase databases was conducted until April 2025. Inclusion criteria were randomized controlled trials and articles published in English, and studies including adult patients under general anesthesia, where anesthetics were titrated using a depth of anesthesia monitor, to determine the incidence of POD or POCD. The quality of relevant articles was assessed using the Cochrane risk-of-bias tool.

Results: After full-text evaluation and quality assessment, ten articles were included in this narrative review. Six out of eight articles found a significant decline in POD when using a depth of anesthesia monitor. In comparison, only one of five studies found a significant decline in POCD. Seven study groups concluded that using a DoA monitoring system led to a decrease in the total dose of anesthetic administered.

Conclusion: Based on the reviewed literature, there may be a beneficial effect on the incidence of POD when a DoA monitor is used during general anesthesia. The effect on POCD seems to be much less significant. DoA monitoring also seems to be useful in lowering anesthetic dosages. However, this subject needs further study in large-scale prospective studies.

Key words: Postoperative delirium, Cognition Disorders, General Anesthesia, Electroencephalography.

Introduction

Postoperative delirium (POD) is a serious and common complication of surgery, associated with significant morbidity and additional health care costs. POD affects older age groups more often and differs among types of surgery, with the highest incidence (33-65%) in patients needing surgery following a hip fracture¹. Delirium is defined according to the Diagnostic and Statistical Manual of Mental Disorders fifth edition (DSM-5) as an acute disturbance in cognition, attention and awareness. It typically develops over a short period of time and can fluctuate during the day². Postoperative cognitive dysfunction

(POCD) overlaps with postoperative delirium, but is considered to occur over a long-term period (months) after hospital discharge. It is defined as a decline in postoperative cognition. However, there is no consensus about the definition³.

Historically, anesthesiologists use clinical parameters such as movement, elevated blood pressure and heart rate to determine the depth of anesthesia⁴. In the transition from an awake to a state of general anesthesia, there are significant changes in the brain's spontaneous electrical activity, which can be recorded on an electroencephalogram (EEG)⁵. During excessively deep levels of general anesthesia burst suppression can occur. This is categorized by a continuous alternation between

high voltage slow waves (bursts) and low voltage activity (suppression)⁶. This burst suppression EEG pattern has been associated with an increased incidence of POD⁷. One study in cardiac surgery, comparing the duration of intra-operative burst suppression between delirious and non-delirious patients, observed a significantly longer time in burst suppression in the delirious group (107 versus 44 minutes respectively)⁸.

In the past decades, the development of depth of anesthesia (DoA) monitors has provided anesthesiologists with the tools for monitoring and maintaining an adequate level of hypnosis. On the one hand, avoiding an excessively deep state of anesthesia with burst suppression can potentially reduce postoperative cognitive complications. On the other hand, it may help minimize the risk of awareness⁵. These DoA monitors use algorithms that are based upon bilateral processed analyses of the EEG, recorded by applying electrodes to the forehead of the patient. Most currently used DoA systems display a dimensionless value correlating with anesthetic depth, usually from zero (deep coma) to one hundred (awake)⁹. The target value for an adequate depth of anesthesia is assumed to be between 40 and 60, for the majority of the DoA monitors. Commonly used and widely available DoA monitoring systems are the Bispectral Index (BIS), Entropy and the NeuroWave. Currently, the use of DoA monitoring during anesthesia is not considered a gold standard in Belgium.

Furthermore, the published literature can sometimes be contradictory. A meta-analysis by MacKenzie et al.¹⁰ from 2018 concluded from three of the included five studies that there was a significant relationship between the use of DoA monitoring and a decreased risk of POD. Overall, they found that the use of DoA monitors, reduced the odds of developing POD by approximately 38%¹⁰. In contrast, Wildes et al.¹¹ found no significant difference in POD when comparing the DoA monitored and standard of care group in their ENGAGES trial.

Objectives

The aim of this review is to explore the currently available literature and assess if the use of DoA monitors could be implemented during general anesthesia to decrease the number of patients developing POD compared to the standard of care. Currently, the use of DoA monitoring is not considered to be part of the standard of care during general anesthesia in Belgium. Secondary aims are to evaluate whether using DoA monitoring could reduce the incidence of POCD and the total dosage

of anesthetic agents used during general anesthesia compared to the standard of care without DoA monitoring.

Methods

An extensive search was conducted by a single reviewer between January and April 2025 using the PubMed and Embase databases. No restrictions were applied to the publication date. A combination of the following keywords were used: “processed electroencephalography”, “processed EEG”, “pEEG”, “depth of anesthesia”, “depth of anesthesia monitoring”, “anesthesia”, “postoperative delirium”, “delirium” and “postoperative cognitive dysfunction”. These keywords were combined with the Boolean operators AND and OR.

The results were screened by the author of this review, based on title and abstract to assess whether they met the inclusion criteria.

Inclusion criteria were: randomized controlled trials (RCTs), articles published in English, and studies involving adult patients under general anesthesia where anesthetics were titrated using a DoA monitor, to measure the effect on the incidence of POD or POCD. Studies not meeting the aforementioned criteria were excluded. The quality of the remaining articles was assessed using the Cochrane risk-of-bias (RoB) tool¹². Articles deemed to have a high overall risk of bias were excluded.

Results

The search of both databases yielded 1304 results in total. After removal of duplicates, 1293 articles were screened based on title and abstract. After the first screening, a total of 20 articles remained for full-text evaluation. Using the Cochrane risk-of-bias tool¹², 10 articles were excluded, of which 4 trials were not randomized. Three publications were excluded because they were scored low in quality, and an additional three articles were deemed not relevant after full-text evaluation. As a result, the remaining 10 articles were included in this narrative review. An overview of the inclusion process is shown in Figure 1. The included articles had a low or moderate overall risk of bias according to the Cochrane RoB tool¹², as depicted in Figure 2. The characteristics of all studies included in this review are listed in Table I.

Postoperative delirium

Eight of the articles examined the incidence of POD^{11,13-19}. Of these, six studies reported a significant decline in POD when using a DoA monitor to titrate

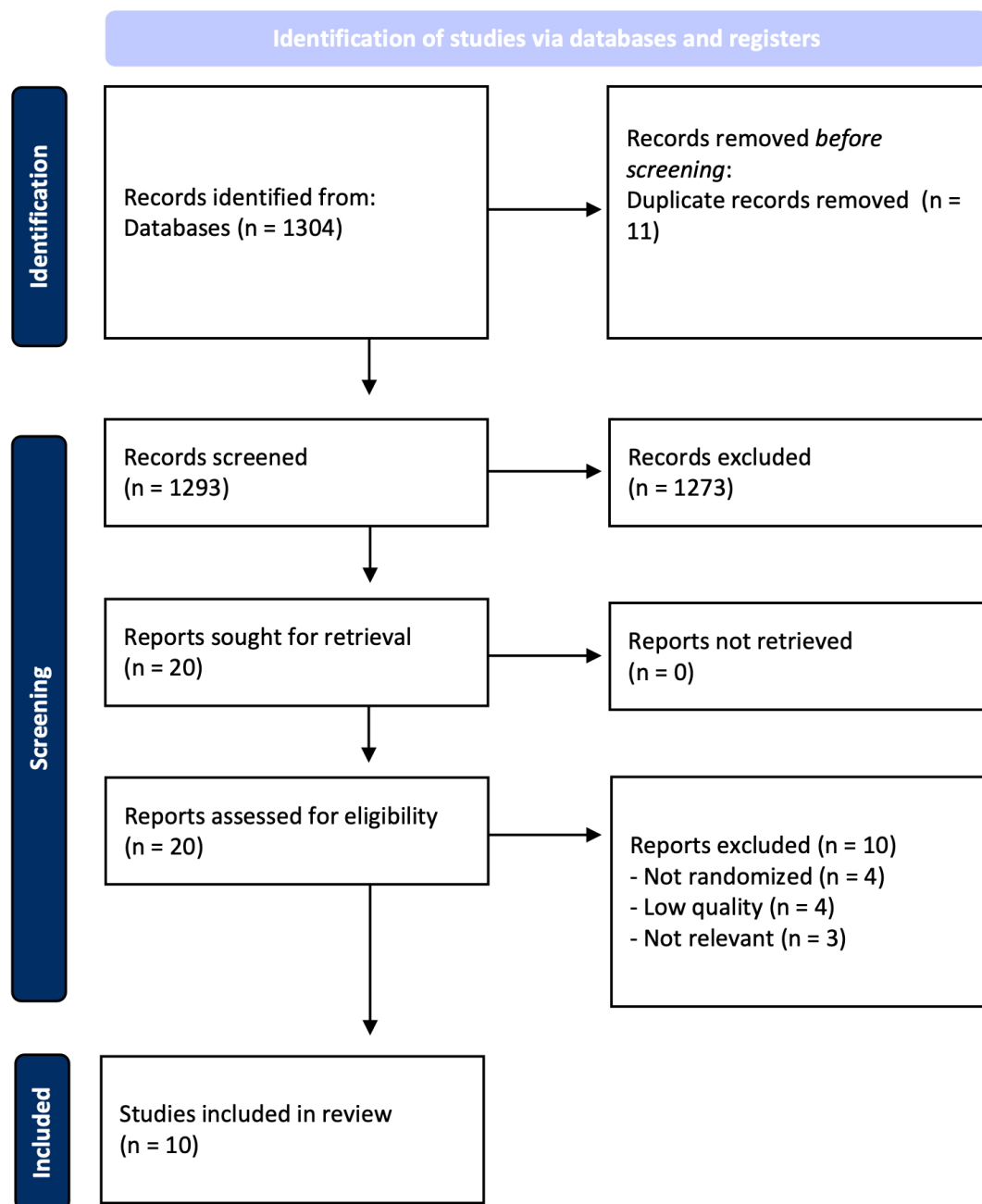


Fig. 1 — PRISMA flow diagram of the inclusion process.

anesthetics during general anesthesia^{13-17,19}. Whitlock et al.¹⁸ also concluded that the use of a DoA monitor reduced the incidence of POD; however, their results were not statistically significant. The ENGAGES trial was the only study included that found no difference in the incidence of POD when using a DoA monitoring system¹¹.

Seven study groups applied the Confusion Assessment Method (CAM)²⁰ or Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) to assess for POD. Only Radtke et al.¹⁷ used a different tool to assess POD, namely the DSM-IV criteria²¹.

An interesting study by Evered et al.¹⁴ exclusively included patients that were defined as American Society of Anesthesiologists (ASA) physical status

class III and IV, who may be at a greater risk of developing delirium. In addition, this is the only study that compared two different specific targets for DoA, striving for a BIS value of 35 in one group and a BIS value of 50 in the other group. Following major surgery, the incidence of POD was 28% in the BIS 35 group and 19% in the BIS 50 group ($p = 0.01$). Interestingly, the patients who developed POD spent an average of five minutes longer in burst suppression than patients who did not¹⁴. The results of these eight studies are summarized in Figure 3, comparing the incidence of POD in the DoA monitored groups versus control (or low BIS) groups. In the standard of care groups the incidence of delirium ranged from 20% to 41%, and in the DoA monitored groups from 2% to 28%^{11,13-19}.

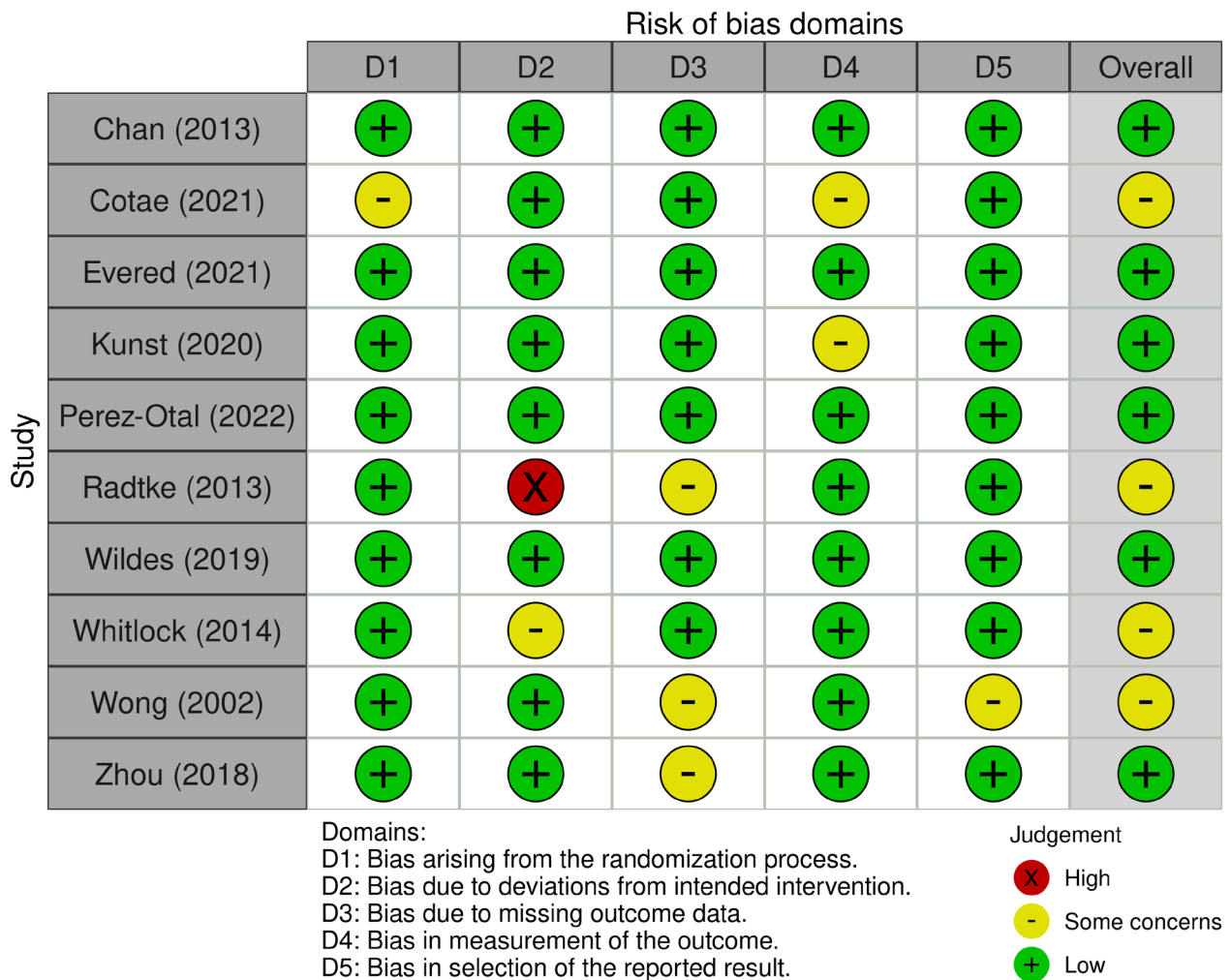


Fig. 2 — Risk of bias plot, generated using the robvis tool²⁷.

Table I. — Characteristics of the included studies.

First Author	Year of publication	Study population	Age (years)	DoA monitor	Main anesthetics used	Type of surgery	Target DoA	Control
Chan ¹³	2013	921	≥60	BIS	Propofol Volatile anesthetics	Major surgery	40-60	Standard practice
Cotae ²²	2021	95	>18	Entropy	Sevoflurane	Abdominal Orthopedic	40-60	Standard practice
Evered ¹⁴	2021	547	≥60	BIS	Volatile anesthetics	Major surgery	35 vs 50	N/A
Kunst ¹⁵	2020	82	≥65	BIS	Isoflurane	CABG on CPB	50 ± 10	Standard practice
Pérez-Otal ¹⁶	2022	204	>65	BIS	Volatile anesthetics	Major surgery	40-60	Standard practice
Radtke ¹⁷	2013	1277	≥60	BIS	Propofol Volatile anesthetics	Mixed elective surgery	No target	Standard practice
Whitlock ¹⁸	2014	310	>18	BIS	Volatile anesthetics	Cardiac Thoracic	40-60	Standard practice
Wildes ¹¹	2019	1232	≥60	BIS	Volatile anesthetics	Major surgery	>40	Standard practice
Wong ²³	2002	68	>60	BIS	Isoflurane	Orthopedic	50-60	Standard practice
Zhou ¹⁹	2018	81	65-75	BIS	Propofol	Colon	40-60	Standard practice

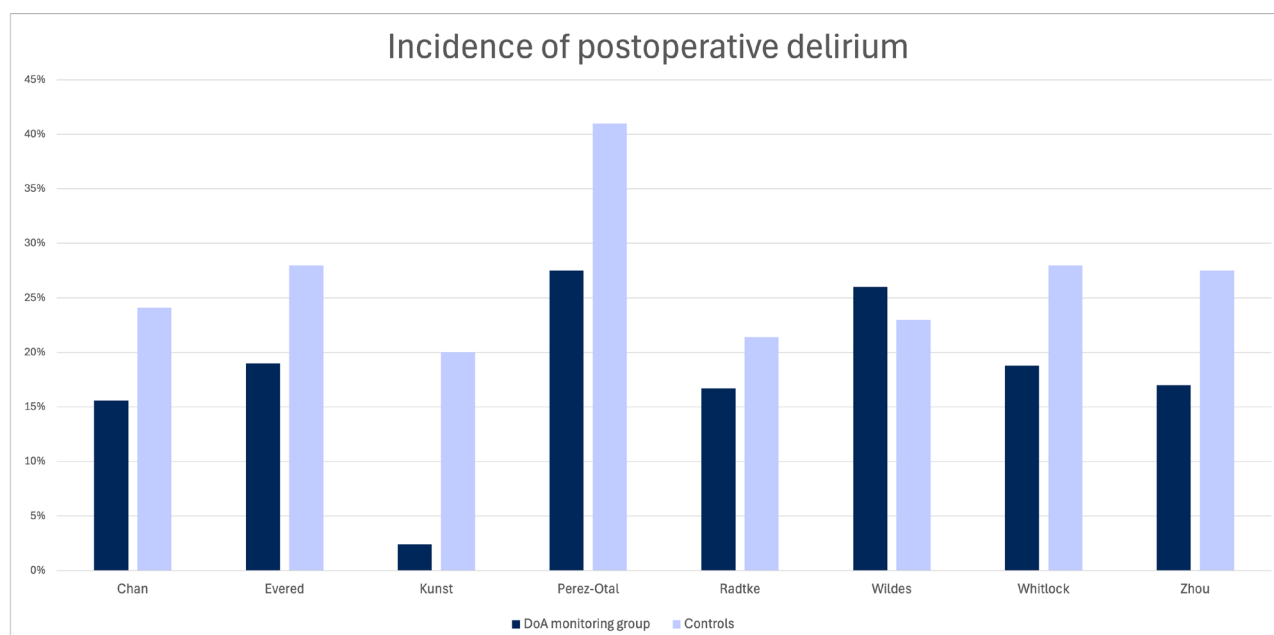


Fig. 3 — Comparison of POD in the DoA monitored groups and control groups. The data were extracted from previously published studies^{11,13-19}. DoA: depth of anesthesia.

Postoperative cognitive dysfunction

Five of the included studies investigated the effect of DoA monitoring on the incidence of POCD^{13,15,17,22,23}. Three study groups found no difference in the occurrence of POCD when a DoA monitor was used^{15,17,23}. Cotae et al.²² found a non-significant decline in POCD when using a DoA monitoring system. Only Chan et al.¹³ found a significant decrease of POCD, namely 10,2% in the BIS monitored group versus 14,7% in the control group.

For the assessment of POCD there was very little overlap between studies, two studies implemented the Mini-Mental State Examination (MMSE)^{15,23}. Wong et al.²³ combined this with the Digit Symbol Substitution Test (DSST) and the Trieger Dot Test (TDT). The three remaining studies used one of the following assessment tools: the Neelon and Champagne (NEECHAM) Confusion Scale, the Cognitive Failures Questionnaire (CFQ), or the Cambridge Neuropsychological Test Automated Battery (CANTAB)^{13,17,22}.

Dosage of anesthetics

Seven articles reported the dosages of anesthetics used in both groups, each of them found that using a DoA monitor reduced the total dose of anesthetic^{11,13,14,18,19,22,23}. Five study groups calculated the p-value, of which four concluded that the reduction in anesthetic dosages was significant^{13,14,19,22,23}. Wong et al.²³ found the volume of isoflurane used during orthopedic surgery to be 30% lower in the BIS group compared with the control group. A study by Cotae et al.²² produced

similar results using sevoflurane. Chan et al.¹³ compared estimated effect site concentrations of propofol. This was estimated to be 2.7 µg mL⁻¹ in the DoA monitored group compared to 3.3 µg mL⁻¹ in the routine care group¹³.

Discussion

Based on the reviewed literature, the use of DoA monitoring to titrate anesthetics may be beneficial in decreasing POD. The large-scale ENGAGES study from 2019 was the only study that found using EEG guidance of anesthesia did not decrease POD¹¹. It was hypothesized that the difference in findings between Wildes et al.¹¹ and Evered et al.¹⁴ might be explained by differing trial execution and characteristics of the study population²⁴. Moreover, in the ENGAGES trial there was no set target in the DoA monitored group - the anesthesiologists were solely encouraged to keep the BIS value above 40 as much as possible. In addition, there are no mean BIS values reported from either study group, so it's possible the difference in DoA between groups was minimal. They concluded that the use of EEG monitoring decreased the time spent in burst suppression¹¹. Moreover, the mechanism explaining this possible association is unknown, and more research is needed to further assess the correlation between the duration of burst suppression and POD.

The study by Radtke et al.¹⁷, comparable in size to the ENGAGES trial, did find a significant decline of 16,7% in POD when using a DoA monitor. Limitations of their study are the facts

that 141 patient from the BIS-blinded group were unblinded at some point during the procedure and that they used the DSM-IV to assess POD instead of the CAM17. Even though the CAM is based on the DSM, the CAM is often preferred in clinical studies due to the practicality and standardization.

Four studies included a study population fewer than 100 patients, therefore, these outcomes should be interpreted with caution^{15,19,22,23}.

In 2023, Sumner et al.²⁵ concluded in their meta-analysis, there was no effect of using DoA monitoring on the incidence of POD with an inverse heterogeneity model. However, after applying a random-effects model, they did find a significant decline in the incidence of POD in the DoA monitored group²⁵. Another meta-analysis by Ling et al.²⁶ concluded that a higher BIS value significantly reduced POD, and POCD at three months. Additionally, there appeared to be substantial heterogeneity among the included studies, and Trial Sequential Analysis (TSA) showed the results regarding POD, but not POCD, were underpowered²⁶.

After studying 921 patients, Chan et al.¹³ concluded that risk factors for developing POD and POCD include older age, high anesthetic dosages, low mean BIS and relatively long periods of the BIS value under 40. This conclusion is supported by the results of the majority of the other studies included in this review.

The link between DoA monitoring and the occurrence of POCD appears even less clear, with only one of the five included studies reporting a significant decline of POCD in the DoA monitored group¹³. This may be explained by the fact that there is no clear definition yet and the tests used to assess POCD were very heterogeneous.

There also seems to be a benefit regarding the anesthetic dosages used during DoA monitored anesthesia, with all seven articles showing a decline in the total anesthetic administered^{11,13,14,18,19,22,23}. However, the significance of this difference was not calculated by every study group.

It should be noted that the possible effects on POD, POCD and anesthetic dosages are probably not a direct result of the DoA monitor itself, but rather of how it influences anesthetic management.

A limitation of this and similar reviews is the fact that the included articles are usually heterogeneous regarding size and composition of the study populations, anesthetic techniques and assessment tools for POD and POCD. Moreover, the fact that it was executed by one single reviewer is a limitation of this specific review as well. Another potential drawback, is the notion that patients with preexisting neurocognitive or psychiatric disorders

were excluded from all included studies; however, these disorders are known predisposing factors for developing delirium¹. In the future, it may be interesting to study the groups that have the highest risk of developing POD and POCD.

Additionally, most articles examined a rather small study population, so conclusions need to be drawn carefully. Moreover, this presents the need for large-scale research on this topic.

In conclusion, the use of DoA monitoring may be useful in reducing the incidence of POD and in reducing the dosage of anesthetics administered. However, further large scale research is needed, and should also specifically focus on patients at high risk of developing POD.

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