



Neurological complications after cardiac surgery: anesthetic considerations based on outcome evidence

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Purpose of review

Neurological complications after cardiac surgery remain prevalent. This review aims to discuss the modifiable and outcome-relevant risk factors based on an up-to-date literature review, with a focus on interventions that may improve outcomes.

Recent findings

There is a close relationship between intraoperative blood pressure and postoperative neurological outcomes in cardiac surgical patients based on cohort studies and randomized controlled trials. Adopting an optimal and personalized blood pressure target is essential; however, the outstanding issue is the determination of this target. Maintaining cerebral tissue oxygen saturation at least 90% patient's baseline during cardiac surgery may be beneficial; however, the outstanding issues are effective intervention protocols and quality outcome evidence. Maintaining hemoglobin at least 7.5 g/dl may be adequate for cardiac surgical patients; however, this evidence is based on the pooled results of thousands of patients. We still need to know the optimal hemoglobin level for an individual patient, which is of particular relevance during the decision-making of transfusion or not.

Summary

The available evidence highlights the importance of maintaining optimal and individualized blood pressure, cerebral tissue oxygen saturation and hemoglobin level in improving neurological outcomes after cardiac surgery. However, outstanding issues remain and need to be addressed via outcome-oriented further research.

Keywords

blood pressure, cardiac surgery, cerebral tissue oxygen saturation, hemoglobin, neurological complications

INTRODUCTION

The significant improvements in both surgical techniques and anesthetic management for cardiac surgery have given millions of individuals who suffer from a life-threatening cardiovascular disease a new chance at life [1]. Although the overall perioperative mortality and morbidity has significantly reduced, neurological complications remain a major concern to this patient population [2,3].

Neurological complications secondary to cardiac surgery encompass a variety of disorders, including stroke, postoperative delirium (POD), and postoperative cognitive decline (POCD) [2,4]. The incidence of overt stroke (clinically symptomatic) ranges from 1.2 to 6%; whereas the covert stroke (clinically silent) detected by diffusion-weighted MRI occurs in as many as 50% of patients [5^{••},6^{••}]. The reported incidence of POD ranges from 14 to 50% in cardiac surgical patients [2]; whereas POCD occurs in 25 to 50% of patients after cardiac

surgery [2,5^{••},7]. These neurological complications are associated with increased mortality, decreased quality of life and increased economic burden [4,8].

The cause of neurological complications is complex, elusive and likely multifactorial. Risk factors that are associated with various neurological complications include, but not limited to, age, history

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KEY POINTS

- Neurological complications after cardiac surgery remain prevalent in modern era.
- The intraoperative blood pressure management should be guided by an optimal and personalized target in cardiac surgical patients.
- Cerebral tissue oxygen saturation should be maintained close to patient's baseline levels during cardiac surgery.
- Hemoglobin should be maintained no lower than 7.5 g/dl in cardiac surgery.

of previous stroke, preexisting cerebrovascular diseases, hypertension, atrial fibrillation, systemic inflammation, and surgical manipulation [6[■],9].

It should be noted that most of the risk factors, such as age and past medical history are not modifiable; whereas some factors, such as hypertension and atrial fibrillation, can be treated, optimized, and regarded as modifiable. The perioperative task is to intervene on those modifiable risk factors to further reduce neurological complications after cardiac surgery. In this review, we discuss those aspects in perioperative care that are modifiable and relevant to neurological complications after cardiac surgery based on the outcome evidence.

OPTIMAL BLOOD PRESSURE AND HEMODYNAMIC MANAGEMENT

The appropriate blood pressure target during cardiopulmonary bypass (CPB) has always been contentious [5[■],6[■],10–12]. Both hypotension and hypertension are deleterious. Hypotension may compromise the clearance of emboli and reduce cerebral perfusion, especially the blood flow to the watershed areas of the brain [13]. Hypertension may lead to postoperative delirium [14]. It is important to keep the blood pressure in an ideal range that is associated with the least neurological complications after cardiac surgery.

It has been common to maintain mean arterial pressure (MAP) during CPB in the range of 50 mmHg [15]. However, this empiric target of MAP has not been adequately validated. In contrast, a few randomized controlled trials (RCTs) suggests that the MAP during CBP should be maintained much higher than 50 mmHg. The RCT, performed in 248 patients undergoing coronary artery bypass grafting (CABG), showed that the strategy of maintaining a higher MAP during CPB (80–100 mmHg) led to a lower incidence of stroke compared with the

strategy of maintaining a lower MAP during CPB (50–60 mmHg) (2.4 versus 7.2%) [10]. A different RCT, performed in 92 patients undergoing CABG, showed that maintaining a higher perfusion pressure during CPB (80–90 mmHg) led to a reduced incidence of POD (0 versus 13%) and a better Mini-Mental-Status scores (1.1 ± 1.9 versus 3.9 ± 6.5) compared with the practice of maintaining a lower perfusion pressure during CPB (60–70 mmHg) [11].

A recent large retrospective cohort study based on 7457 cardiac surgical patients showed that there is a strong association between sustained MAP of less than 64 mmHg during CPB and postoperative stroke [6[■]]. During CPB, every additional 10 min of MAP less than 55 mmHg was associated with a 16% increase in the odds of stroke, whereas every additional 10 min of MAP between 55 and 64 mmHg was associated with a 13% increase in the odds of stroke [6[■]]. This study suggests that both the severity and the duration of hypotension during CPB are associated with the risk of stroke after cardiac surgery. Although this study suggests that the MAP should be maintained no lower than 64 mmHg during CPB, it does not inform the most ideal MAP range for this population and for individual patient in this population.

Not every study supports the linkage between a higher perfusion pressure during CPB and favorable neurological outcomes in cardiac surgery. A prospective cohort study based on 734 cardiac surgical patients did not find an association between intraoperative hypotension (MAP <50 mmHg, MAP decrease >30% relative to the baseline or MAP decrease >40% relative to the baseline) and POD [12]. The recent Perfusion Pressure Cerebral Infarcts (PPCI) RCT investigated the effect of maintaining a higher (70–80 mmHg) versus a lower (40–50 mmHg) blood pressure during CPB on postoperative brain injury diagnosed using diffusion weighted imaging [5[■]]. This trial found that using norepinephrine to maintain a higher blood pressure did not reduce the incidence and severity of cerebral injury [5[■]]. It must be noted that, although blood pressure was different, pump flow during CBP was maintained at the same level (2.4 l/min) for both groups in this trial. Although this study has some limitations, it challenges the findings of many previous studies [16[■]].

Another direction of research is to define the optimal cerebral perfusion pressure based on cerebral pressure autoregulation, a mechanism that maintains a stable cerebral blood flow in the face of a fluctuating blood pressure [17]. However, cerebral autoregulation varies both inter-individually and intra-individually secondary to a variety of factors [18–20]. Cerebral autoregulation may also vary during a cardiac surgical procedure [21[■]]. This

variation challenges the practice of maintaining the MAP within the autoregulatory range. The solution may be to guide the clinical care using a monitor that continuously assesses cerebral autoregulation.

Using a moving Pearson correlation coefficient between MAP and the mean middle cerebral artery blood flow velocity or cerebral oxygen saturation, cerebral autoregulation can be assessed using mean velocity index (Mx) [22] or cerebral oximeter index (Ox) [23]. In a prospective observational study performed in 232 patients undergoing CABG, Joshi *et al.* [24] determined that the average lower limit of cerebral autoregulation in their patient population was 66 mmHg based on the Ox method. This value is higher than the traditionally used 50–60 mmHg threshold [17]. Importantly, the range of the lower limit of cerebral autoregulation has a wide distribution from 43 to 90 mmHg. It implies that it is easy to underestimate or overestimate the lower limit of cerebral autoregulation in an individual patient if it is not directly monitored.

In another study of 614 patients having cardiac surgery, Joshi *et al.* found a strong association between the product of the magnitude and duration of hypotension (by referring to the lower limit of cerebral autoregulation) and the risk of postoperative stroke based on the Mx method [25]. They showed that the lower and upper limits of cerebral autoregulation were 65 and 84 mmHg, respectively, with the optimal MAP at 78 mmHg, during CPB in their patient population [25]. They additionally showed that 17% of their patients had a lower limit of cerebral autoregulation above whereas 29% of their patients had an upper limit of cerebral autoregulation below the optimal MAP of 78 mmHg [25]. This finding suggests that even the optimal MAP for a patient population may underestimate or overestimate the optimal MAP for an individual patient.

These studies suggest that personalized MAP management based on a real-time cerebral autoregulation monitor deserves further exploration. An RCT (Cerebral Autoregulation Monitoring During Cardiac Surgery) comparing the conventional MAP management versus Mx and Ox-guided MAP management in cardiac surgery is currently ongoing (NCT00981474).

In summary, both hypotension and hypertension during cardiac surgery are detrimental to cardiac surgical patients. Optimized blood pressure management based on a personalized target is promising in further improving neurological outcomes after cardiac surgery. The outstanding question that remains to be answered is how to identify this target in an individual patient. The best hemodynamic management based on flow parameters, such as cardiac output or pump flow remains elusive.

CEREBRAL OXYGENATION-GUIDED CARE

Central nervous system can be monitored by a number of methods including processed electroencephalography and cerebral tissue oxygen saturation (SctO₂) based on near-infrared spectroscopy [26,27]. The value of SctO₂ is essentially determined by the balance between cerebral tissue oxygen consumption and supply [28]. The role of SctO₂ monitoring in recognizing cerebral desaturation and improving neurological outcomes after cardiac surgery has been extensively studied [29–31,32[■]].

In a prospective observational study performed in cardiac surgical patients, Yao *et al.* [33] found an association between intraoperative cerebral desaturation and postoperative neurological complications assessed based on a simplified antisaccadic eye movement test and Mini-Mental State Examination. In a secondary analysis of a prospective randomized trial, Holmgaard *et al.* [34[■]] found a significant difference in SctO₂ measurements between patients with or without new cerebral ischemic lesions after cardiac surgery. The effects of SctO₂-guided intraoperative care on neurological complications after cardiac surgery have been investigated [29,30,35]. The results showed that, when SctO₂ was maintained at least 75% baseline [30], at least 80% baseline [35], or near patient's baseline [29], there were fewer strokes [29,30] and a lower incidence of POCD [35]. These interventional studies suggest a causal relationship between a low SctO₂ and neurologic complications after cardiac surgery and highlight the importance of maintaining an optimal intraoperative SctO₂.

Not every study found a favorable effect exerted by SctO₂-guided care on neurological outcomes after cardiac surgery [32[■]]. In a recent RCT ($n = 249$), Lei *et al.* [32[■]] found that the incidence of POD was similar in patients with and without cerebral desaturation, as well as in patients with restored and not restored SctO₂.

The cause of these diverse results remains to be reconciled. It may be due to the variations in SctO₂ thresholds used for intervention, the success rates in maintaining SctO₂ at the target level, outcome measures, and patient characteristics [3,6[■],29,30,34[■],35]. The SctO₂ threshold used for intervention was 75% baseline in Murkin *et al.*'s [30] study, and 80% baseline in Colak *et al.*'s [35] study. In Lei *et al.*'s [32[■]] study, the intervention algorithm was commenced when SctO₂ was less than 75% baseline for 1 min. They had an 80% success rate in maintaining SctO₂ at the target level. The success rate in maintaining SctO₂ at 90% baseline or above was much higher (97%) in the pilot study performed by Deschamps *et al.* [31].

At this time, it appears reasonable to apply a SctO₂ monitor in cardiac surgical patients. It may be

ideal to maintain SctO₂ above 90% baseline. The intervention options include verification of head/neck position, inspection of different cannulas, increasing MAP, cardiac output or pump flow, and FiO₂, avoiding hyperventilation and 'light' anesthesia, and red blood cell transfusion [31,35].

RED BLOOD CELL TRANSFUSION AND THE OPTIMAL HEMOGLOBIN LEVEL

Anemia is deleterious. Two large cohort studies ($n=17\,056$ and $10\,949$, respectively) demonstrated that anemia is associated with increased risk of stroke after cardiac surgery [36,37]. Severe anemia can compromise cerebral oxygen delivery, which may adversely affect the wellbeing of the brain [38].

On the contrary, red blood cell (RBC) transfusion may exert an adverse neurological effect in patients having cardiac surgery [39,40]. Patients receiving one to two units of RBC transfusion had a three-fold to four-fold increase in the risk of stroke or transient ischemic attack after cardiac surgery, and this negative effect was independent of the surgical type and the typical predictors for perioperative stroke following the adjustment by the multilevel propensity score [41]. The potential underlying mechanisms include impaired oxygen delivery at the cellular level, prothrombotic events secondary to morphological abnormalities of packed RBCs, and the release of deleterious substances from packed RBCs [41,42].

It is important to maintain hemoglobin at a level that is adequate for tissue oxygen supply, and at the same time, minimize the hazards associated with RBC transfusion. The transfusion target in cardiac surgery was a hematocrit of 20–24% based on the previous studies [5[■],11]. The two recently published articles by Mazer *et al.* [43,44[■]] reported that a restrictive transfusion threshold (Hb <7.5 g/dl, $n=2430$) was not inferior to a liberal transfusion threshold (Hb <9.5 g/dl, $n=2430$) in cardiac surgery based on outcome measures including postoperative stroke. Nonetheless, the optimal and individualized hemoglobin level in cardiac surgical patients still deserves more research.

OTHER PROMISING DIRECTIONS

Epi-aortic ultrasound is recommended before cannulation in cardiac surgery [45]. It can identify atherosclerotic lesions in the ascending aorta and allows for surgical adjustment aimed at preventing atherogenic emboli. The available evidence suggests that it may reduce the incidence of stroke in cardiac surgical patients [46–48]. Dexmedetomidine is reported to be able to reduce the incidence and duration of delirium after cardiac surgery [49,50].

CONCLUSION

Cardiac surgical patients are prone to various neurological complications. Endeavors should be made to identify those modifiable risk factors and investigate if relevant interventions can effectively reduce the incidence of various neurological complications after surgery. The available evidence suggests that maintaining an optimal and personalized blood pressure, SctO₂ close to the baseline level, and hemoglobin above 7.5 g/dl during cardiac surgery may improve neurological outcomes after surgery. Further research, especially quality outcome-oriented RCTs, is needed to improve the perioperative care including neurological outcomes after cardiac surgery.

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Conflicts of interest

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- of special interest
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