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# THE EFFECT OF INTRAOPERATIVE BLOOD PRESSURE FLUCTUATIONS ON POSTOPERATIVE DELIRIUM AFTER CARDIAC SURGERY

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## ABSTRACT

**Background:** Postoperative delirium (POD) is a common postoperative neurocognitive complication following cardiac surgery, which leads to prolonged hospital stay and recovery. The study is focused on the relationship between IOBPV and POD, suggesting that BP fluctuations could be a risk factor for neurological outcomes. **Patients:** Sixty adult patients were selected from Ibn Al-Bitar Center and Iraqi Centers for Cardiac Surgery in Baghdad and subjected to cardiac surgeries between August–November 2018, excluding patients with significant pre-existing neurological and psychiatric disorders. The definition of significant BP fluctuations in this study was when the BP was more than 20% from baseline for more than 15 minutes; or required the use of vasoactive agents. Delirium was rated according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria and validated instruments following surgery. **Results:** Mean age was 52.4±13.6 years, and 38 (63.3%) patients were male. Thirty-six (60.0%) patients had BP fluctuations. POD developed in 30 (50.0%) patients. 22/36 (61.1%) of the patients with BP fluctuations had POD, while 8/24 (33.3%) of the patients without BP fluctuations had POD ($p=0.03$). In addition, age >60 years and a female sex were significantly associated with POD ($p=0.03$ for both). Diabetes mellitus was not statistically significant ($p=0.20$) and surgical procedure was not significantly associated with POD. **Conclusion:** This study suggests a strong relationship between changes in intra-operative blood pressure and the incidence of postoperative delirium (POD) after cardiac surgery. The study underscores the importance of systematic hemodynamic monitoring, personalized blood pressure regimen, preoperatively evaluating delirium risk, and organized postoperative monitoring. More studies are required to establish causality and selected targets of the hemodynamics.

**KEYWORDS:** Postoperative Delirium, Cardiac Surgery, Blood Pressure Variability.

## INTRODUCTION

There have been significant advances in operative technique, cardiopulmonary bypass (CPB), myocardial protection, anesthesia, intensive care, and postoperative rehabilitation in cardiac surgery. However, neurological and neurocognitive complications are clinically significant outcomes of cardiac surgery. One of these complications is postoperative delirium (POD) which can present acutely, be variable and significantly impact recovery. There are multiple potential precipitating factors in cardiac surgical patients such as CPB, systemic inflammatory activation, embolic phenomena, blood loss, transfusion, postoperative mechanical ventilation, metabolic disturbances, pain, sleep disruption and exposure to sedative medications. Numerous predisposing (intrinsic) and precipitating (extrinsic) factors have been identified in systematic reviews after cardiac surgery, highlighting that POD is a multifactorial syndrome and not the result of one single insult.[1-4]

Delirium is a disturbance of attention and a Further disturbance of cognition not accounted for by a previous neurocognitive disorder, and occurring with the disturbance of attention. It is characterized by acute or subacute onset and a fluctuating course.[5] Delirium can be especially challenging to detect in postoperative and ICUs where hypoactive patients may be quiet and sleepy, or cooperative, but not obviously agitated. This may be under-diagnosis and delayed intervention if this subtype is not identified.

POD is not just a post-surgical phenomenon. Delirium may be associated with extended intensive-care and hospital stays, greater complications, diminished functional recovery and enhanced mortality rates. Age, preexisting cognitive impairment, cerebrovascular disease, depression, atrial fibrillation, prolonged mechanical ventilation, transfusion and postoperative complications have consistently been shown to be associated with delirium in cardiac surgery populations.[1-4] In a recent meta-analysis, involving over 13,000 cardiac surgical patients, a number of factors were found to be important risk factors, including age, diabetes, depression, mild cognitive impairment, carotid disease, longer time spent on mechanical ventilation, and longer time spent in the intensive care unit (ICU).[6]

Some of the risk factors are not modifiable, but the intraoperative hemodynamic management of patients is a potentially modifiable part of perioperative management. The cerebral perfusion pressure is closely linked to blood pressure, and the cerebral blood flow is regulated over varying arterial pressures by an intrinsic mechanism called cerebral autoregulation. But different people have different levels of autoregulatory ability and some pathologic states (such as advanced age, chronic hypertension, vascular disease, diabetes) can diminish the ability to autoregulate.[7,8]

The introduction of CPB introduces further complexities as it alters the normal physiologic relationships between arterial pressure and flow, between vascular resistance and flow, between hematocrit and blood flow, between temperature and flow, and between the delivery of oxygen to the brain and the oxygen delivery capabilities of the circulatory system. The arterial pressure can drop below or increase above an individual's autoregulatory range during CPB. Importantly, a patient may have a different autoregulatory limit and keeping the MAP target within the empiric zone does not ensure adequate cerebral perfusion. However, observational studies have shown that both inadequate and excessive arterial pressure during CPB above the cerebral autoregulatory range may also have clinical significance with respect to postoperative delirium.[9]

Blood pressure variability could thus prove to be a valuable tool in addition to isolated BP drop. The patient who is in and out of hypotension and hypertension may be experiencing more stress as a result of their fluctuations in blood pressure, even if their average MAP is the same as another patient whose blood pressure is more stable. In a study of 594 older surgical patients, Hirsch et al. studied this concept, and found that absolute or relative hypotension alone during surgery did not appear to be a significant predictor of postoperative delirium, but intraoperative BP variance was.[10] They conclude that the occurrence of hemodynamic instability could be of clinical significance not only because of low pressure, but because of repeated changes in pressure conditions affecting cerebral perfusion.

There has since been a growing body of evidence for this particular aspect in cardiac surgery. Recent investigations with quantitative parameters (standard deviation, average real variability) have shown that there is a relationship between POD and BP variability.[11] Near-infrared spectroscopy (NIRS) has also been used in research to suggest clinically relevant information about cerebral autoregulation during cardiac surgery between MAP and cerebral oxygenation.[12,13] A randomized clinical trial comparing individualized MAP targeting to cerebral autoregulation also showed the feasibility of an autoregulation-guided strategy, but the clinical consequences of this need to be further investigated.[14]

The present study was, therefore, performed to examine the relationship between the intraoperative BP fluctuations and early POD in Iraqi cardiac surgical patients. The study is clinically relevant since treatment of BP is regularly carried out by the anesthesiologist and perfusion team and can potentially be adjusted without substantial changes to the surgical procedure. The main hypothesis was that patients who had large BP changes during surgery would be more likely to develop postoperative delirium (POD) than patients with relatively stable hemodynamics during surgery. Secondary objectives included investigating the relationships between POD and selected demographic and clinical (medical and surgical) factors, such as age, sex, diabetes mellitus, and surgical procedure.

## MATERIALS AND METHODS

### Study Design

A prospective observational clinical study was performed to study the relationship between intraoperative BP fluctuations and POD following cardiac surgery. The study was done from August to November 2018 in both Ibn Al-Bitar Center for Cardiac Surgery and Iraqi Centers for Cardiac Surgery in Baghdad, Iraq.

### Study Population

They included 60 adult patients who received cardiac surgery.

The surgical procedures performed were:

Coronary artery bypass grafting (CABG).
Replace or repair valves.
Surgery for a ventricular septal defect (VSD).
The study population was a consecutive clinical cohort based on the study records.

**Inclusion Criteria**
Those patients who met the following criteria:
1. Were aged ≥18 years.
2. Were to undergo significant cardiac surgery.
3. Had undergone cardiac surgery such as CABG, valve surgery or VSD repair.
4. Given informed consent (either personally or by appropriate proxy if applicable).

Entries were excluded for the following: Patients with Previous major ischemic or hemorrhagic stroke, Transient ischemic attack or established major neurocognitive disorder, Advanced dementia, Severe active psychiatric disease likely to interfere with postoperative assessment, Uncompensated hepatic or renal failure, Severe communication, visual, or auditory impairment preventing reliable cognitive assessment.

**Anesthetic Management:** General anesthesia was used as per cardiac anesthetic guidelines of the institution. Induction agent used were propofol or midazolam with fentanyl or sufentanil. Rocuronium or cisatracurium was used to achieve neuromuscular blockade. Balanced anesthesia (Volatile anesthetic agents, isoflurane or sevoflurane, opioid analgesics and oxygen/air mixtures as needed) Invasive arterial pressure monitoring was achieved by either radial or femoral arterial cannulation.

**Intraoperative Monitoring**
These monitoring modalities were used regularly.
- Five-lead electrocardiography.
- Pulse oximetry.

Arterial lines (invasive).
- Central venous pressure.
- Core temperature monitoring.
- End-tidal carbon dioxide.
- Volatile anesthetic concentration.

CPB parameters (if applicable).
In the CPB period, the pump flow was kept at the level of institutional perfusion practice, which was approximately 2.2-2.4 L/min/m2.
Intraoperative BPF defined as excessive fluctuations of BP during surgery. Intraoperative BPF is defined as: Excessive fluctuations of BP during surgery.
In this study, any significant BP fluctuation was considered as an uncontrolled change in SBP or MAP of more than ±20% from baseline BP measured before induction of anesthesia that lasted for more than 15 minutes, and was deemed significant.
Multiple episodes of hypertension and hypotension, necessitating multiple doses of vasoactive drugs were also taken as evidence of significant hemodynamic fluctuation.

The patients were then divided into.
Group I: BP fluctuates.
Group II: No change in BP.
This definition was created for the purpose of this study, and should not be viewed as a universally agreed upon definition of BP variability.

**Delirium Assessment**
Neurologic/cognitive evaluation was started on the first postoperative day.
Assessment was done in the morning and evening during the clinical evaluation, and until the patient was discharged from the hospital or until the seventh day after surgery, whichever came first.

Diagnosis of delirium was made using the following structured questionnaires along with the DSM-5 clinical criteria.
- CAM-ICU.
- Nu-DESC.
- 4AT.

The 4AT assesses
1. Alertness.
3. Explain the various parts of the AMT.
3. Attention.
4. Sudden alteration of course or change in course.

The 4AT is a validated screening tool with good diagnostic accuracy in various clinical settings (23). A score of ≥4 considered suggestive of delirium in the study protocol.

**Postoperative Cognitive Dysfunction**
The postoperative cognitive dysfunction was recorded when clinically significant postoperative cognitive deterioration was noted and the patient did not meet criteria for delirium. In the present study, the term should be used with caution, as contemporary definitions for PNDs focus on objective neuropsychological assessment before and after surgery.In the present study, the term should be used with discretion unless there was standardized, formal neuropsychological testing both pre and post-surgery.

**Statistical Analysis**
IBM SPSS Statistics was used to analyze data. Data for continuous variables were presented as Mean ± standard deviation. Categorical variables were described in terms of frequencies and percentages. The relationships between categorical variables were evaluated by Pearson's chi-square test. Fisher's exact test was applied in the cases of small expected cell counts. A $p<0.05$ was regarded as statistically significant in this study.

## RESULTS

### *Demographic and Clinical Characteristics*

A total of 60 adult patients were included in the study and as is shown in the table (1) the mean age was 52.4 ± 13.6 years. There were more males in the cohort (63.3%) than females (36.7%). CABG was the most common procedure (66.7%). Valve procedures were 30.0% and VSD repair was 3.3%. In 36 patients (60.0%), there was significant fluctuation in the intraoperative BP. Overall, 30 patients (50.0%) developed POD.

**Table 1: Baseline demographic and clinical characteristics.**

| Parameter | Value |
|---|---|
| **Age/ year/ Mean± SD** | 52.4±13.6 |
| **Male/ No. (%)** | 38 (63.3%) |
| **Female/ No. (%)** | 22 (36.7%) |
| **Body weight/kg/ Mean± SD** | 77.6±18.3 |
| **Diabetes mellitus, n (%)** | 21 (35.0%) |
| **CABG/ No. (%)** | 40 (66.7%) |
| **Valve surgery/ No. (%)** | 18 (30.0%) |
| **VSD repair/ No. (%)** | 2 (3.3%) |
| **Intraoperative BP fluctuation/ No. (%)** | 36 (60.0%) |
| **Postoperative delirium/ No. (%)** | 30 (50.0%) |
| **Postoperative cognitive dysfunction No. (%)** | 21 (35.0%) |

### *Association Between Demographic Variables and POD*

Table (2) showed that there was a significant difference between patients' age groups (p=0.03) regarding POD, with patients above 60 years experiencing a higher prevalence of POD. There was a higher observed proportion of POD in female patients than male (15/22 (68.2%) women vs 15/38 (39.4%) men; p=0.03). There was no statistical association between POD and DM (p=0.20). There was no statistical significance in the distribution of POD by surgical procedure.

**Table (2): Correlation between patient characteristics and postoperative delirium.**

| Characteristic | Total n | Delirium n (%) | No delirium n (%) | p-value |
|---|---|---|---|---|
| **Age >60 years** | 24 | 16 (66.7) | 8 (33.3) | **0.03** |
| **Male** | 38 | 15 (39.4) | 23 (60.6) | **0.03** |
| **Female** | 22 | 15 (68.2) | 7 (31.8) | |
| **Diabetes mellitus** | 21 | 12 (57.1) | 9 (42.9) | 0.20 |
| **CABG** | 40 | 23 (57.5) | 17 (42.5) | 0.08 |
| **Valve surgery** | 18 | 6 (33.4) | 12 (66.6) | 0.07 |
| **VSD repair** | 2 | 1 (50.0) | 1 (50.0) | 0.70 |

### Primary analysis on blood pressure fluctuation and delirium.

Of the 36 patients who had marked intraoperative BP changes, 22 (61.1%) had POD. Eight of 24 patients (33.3%) without significant BP fluctuation had POD compared to no patients in the other group. Therefore, the absolute difference in the POD incidence between the two groups was ~27.8 percentage points. This association was statistically significant (p=0.03). Patients with severe intraoperative BP changes were found to be about 1.83 times as likely to have POD as those without, or a crude risk ratio of 1.83. Table (3) presents this estimate as an exploratory estimate and not as a definitive causal effect because this was an observational study with a small sample size.

**Table 3: Association between intraoperative BP fluctuation and POD.**

| Hemodynamic group | Total n | Delirium n (%) | No delirium n (%) | p-value |
|---|---|---|---|---|
| **BP fluctuation** | 36 | 22 (61.1) | 14 (38.9) | **0.03** |
| **No BP fluctuation** | 24 | 8 (33.3) | 16 (66.7) | |
| **Total** | **60** | **30 (50.0)** | **30 (50.0)** | |

## DISCUSSION

In the present study, 60 adult patients undergoing cardiac surgery were included. The mean age is 52.4±13.6 years, comprising 63.3% males and 36.7% females. The most common procedures performed were CABG (66.7%), valve surgery (30.0%) and VSD repair (3.3%). In 35.0% of patients, diabetes mellitus was present and in 60.0% of the patients, the blood pressure (BP) fluctuated significantly during surgical procedures. In all, 50.0% of the patients experienced postoperative delirium (POD) and 35.0% had postoperative cognitive dysfunction (PCD).

In the current study, the higher prevalence of POD found compared to other studies is indicative of an ongoing recognition of delirium as a significant neurologic complication of cardiac surgery. A recent systematic review and meta-analysis of 27 studies and 5,126 cardiac surgery patients found an overall POD incidence of 25.1% and delirium typically occurred during the first few postoperative days.[15] This incidence percentage (50.0%) is therefore higher than the pooled estimate reported in this meta-analysis. This disparity could be due to the nature of the study population, the surgical procedure, the pre and post-surgical care, the way delirium was assessed, screening for postoperative delirium, and the definition of delirium. The sample size in the present study was relatively small, which might also lead to a less stable estimate of incidence. However, these results highlight the clinical significance of early postoperative vigilance for delirium in cardiac surgical patients.

The average age of the population in this study was 52.4 ± 13.6 years. In the present study, age was a significant predictor of POD despite being a relatively young cardiac surgical population compared to many other studies on POD. Patients >60 years old were significantly more likely to develop delirium (16/24, 66.7%) than were younger patients (p=0.03). This is in line with previous findings which recognized advanced age as an important risk factor for postoperative neurological complication. Roach et al. found that the incidence of postoperative neurological events was significantly higher with increasing age in a prospective study of 2,000 patients who underwent coronary artery surgery, with a 0.9% incidence in patients younger than 65 years, a 3.6% incidence in patients aged 65-74 years, and an 8.9% incidence in patients aged 75 years or older.[16] A similar study of patients receiving CPB also showed that age was an independent risk factor for delirium with an odds ratio of 1.08 for every increase in age.[17] Our results corroborate the findings of the present study, which showed that POD occurred more frequently in older patients.

The association between age and delirium can be explained by several age-related changes in the central nervous system. The cerebral physiological reserve is decreased in older patients, with higher prevalence of vascular disease, impaired cerebral autoregulation and higher susceptibility to inflammatory, metabolic and hemodynamic disturbances. The cardiac surgical procedure can induce additional stress on these mechanisms for example by the use of cardiopulmonary bypass, changes of cerebral blood flow, systemic inflammation and sedative/analgesic treatment. Therefore, normal physiological fluctuations that occur during or following surgery could cause clinically important cerebral dysfunction in older patients. This important relationship of age and POD in this study is therefore biologically plausible and consistent in the literature.

In the current cohort, sex was also found to be significantly associated with POD. Women had a significantly higher number of delirium patients, 15/22 women (68.2%), versus 15/38 men (39.4%) (P=0.03). This discovery implies that vulnerability in females on the basis of sex may be a key factor in this population. Literature, however, regarding sex as an independent risk factor for postoperative delirium is less consistent than for the evidence of age. There were reports of more early complications following CABG in women than men. After adjusting for various baseline cardiovascular risk factors, Brandrup-Wognsen et al. observed that female patients had higher rates of early postoperative morbidity after CABG.[18] In that study, female patients were also more likely to have multiple comorbidities such as diabetes, hypertension, heart failure, renal dysfunction and obesity.[18] These differences suggest that there might be some sex-related differences in baseline risk factors that contribute to the differences in postoperative outcomes.

Therefore, the results of the present study should be interpreted with caution, because POD was more prevalent in females. There were relatively few female patients (n=22) and delirium events among female patients (n=15). Thus, the observed relationship may be due to sampling variation and to other factors not accounted for in the present analysis. However, the discovery is clinically relevant and needs to be further studied in a larger group of patients. Further study is needed to see if female sex is an independent predictor of POD, after adjusting for age, comorbidities, surgery type, the length of cardiopulmonary bypass, transfusion, hypotension, and other perioperative factors.

In the present study, 21 (35.0%) patients had diabetes mellitus. 12 of the 21 patients (57.1%) developed POD, but there was no statistical association between diabetes and delirium (p=0.20). Therefore, there was not enough evidence provided in the present study to confirm the correlation between diabetes and POD. This negative finding does not necessarily contradict previous research. Instead, it could simply be due to the small sample size and statistical power of the current study.

There are some studies which have suggested the relationship of diabetes and postoperative neurological complications. In the patients' undergoing cardiopulmonary bypass, Shirvani et al. reported that diabetes mellitus was an independent predictor of postoperative delirium (odds ratio ~ 3.0, 17). The same study also revealed that patients with postoperative hyperglycemia and electrolyte abnormalities were also associated with delirium.[17] Moreover, in a large retrospective cohort of cardiac surgery patients Choi et al. found that higher glycemic variability during surgery was correlated with a progressively higher incidence of POD, with patients in the highest quartile of glycemic variability having significantly higher odds of delirium than were patients in the lowest quartile.[19] These results indicate that the metabolic effects of diabetes (including perioperatively glucose instability) may be more relevant than the fact of having a diagnosis.

The lack of statistically significant association between diabetes and POD in this limited sample population may suggest that diabetes alone was not a sufficiently powerful discriminator, while details of the actual glucose levels during the perioperative period, glucose variability, renal function, or other metabolic changes may be more discriminating. A binary diabetes variable doesn't reflect the severity or control of diabetes which is important. Therefore, future studies should take other metabolic parameters (HbA1c, glucose variability during the surgery, postoperative hyperglycemia, etc.) into multivariable models.

Cardiac surgery performed included CABG (66.7%), valve surgery (30.0%) and VSD repair (3.3%). The incidence of POD was more common among patients who have undergone CABG (57.5%) than patients who have undergone valve surgery (33.4%) or VSD repair (50.0%). The differences were not statistically significant, however. Thus the present data do not validate surgical procedure as an independent predictor of POD.

Although the proportion of coronary surgery procedures is relatively high, it is still relevant because coronary surgery is highly represented in the literature regarding post-operative neurological complications. There are several mechanisms of cerebral injury that are at risk during cardiac surgery: microembolization, systemic inflammatory response, cerebral perfusion changes, decreases in oxygen delivery, and metabolic abnormalities. The risk might also differ based on the complexity and length of the surgical procedure. One of the factors identified by Roach et al. as important predictors of postoperative neurological events after coronary surgery was the duration of CP bypass.[16] Thus, although in the present study, operative categories were not significant, more detailed operative parameters, such as duration of cardiopulmonary bypass, aortic cross-clamp time, transfusion and intraoperative hemodynamic instability, may give more informative measurements of the perioperative neurological risk.

Among the most significant results of this study, the relationship between intraoperative BP fluctuation with POD was noted. In 36 patients (60.0%), the BP fluctuated significantly during surgery. Of these, 22 patients (61.1%) with POD were present compared to 8 patients (33.3%) without a significant change in BP. So, the difference in delirium rates, when absolute, was ~27.8 percentage points. Patients with significant BP fluctuation had an observed crude risk ratio of ~1.83, suggesting the observed risk of POD was ~1.8 times higher for patients with significant BP fluctuation than for those without significant BP fluctuation. Association was significant (p=0.03).

This discovery is of significance, as adequate and stable cerebral perfusion is part of cerebral protection during cardiac surgery. Changes of blood pressure could affect cerebral blood flow, especially in those patients who have impaired cerebral autoregulatory function due to old age, hypertension, atherosclerosis, diabetes, or previous cerebrovascular disease. Episodes of hypotension can decrease cerebral perfusion below an individual's autoregulatory range, while high variability can subject the brain to repeated changes in perfusion pressure. These disturbances could lead to cerebral hypoperfusion, decrease in oxygen delivery and ultimately to postoperative neurological dysfunction.

The results from the present study are consistent with recent research that has focused on BP variability during cardiac surgery. A large observational study of 2164 cardiac surgical patients showed that BP variability after surgery was related to POD and suggested that a relatively stable BP level following cardiac surgery would be helpful in reducing the risk of delirium.[20] Most importantly, that study found that BP variability has various relationships with delirium at different levels and moments of BP, and thus BP variability is not a straight-forward exposure and should be best measured with a standardized measurement.

Support for this includes a recent detailed systematic review of 15 studies and 16,407 cardiac surgery patients. The authors found about a 15% higher rate of POD with BPV, and a number of adverse events were correlated with BPV, such as cognitive dysfunction.[21] The review also highlighted the importance of establishing standard definitions and thresholds for BP variability, however. This is of particular relevance in the current study, as the categorisation of patients as having "significant BP fluctuation" might not be directly comparable to studies where BP variability has been quantified using standard deviation, coefficient of variation or average real variability.

Studies on cerebral oxygenation also provide support for the association between BP instability and postoperative neurocognitive complications, showing a biological plausibility. A systematic review and meta-analysis of RCTs in cardiovascular surgery revealed that regional cerebral oxygen saturation monitoring and correction associated with a decrease in postoperative cognitive dysfunction.[22] The authors conclude that the cerebral delivery of oxygen is a key factor in the perioperative neuroprotection and may account for why significant hemodynamic instability can be a risk factor for postoperative neurological complications.

However, the findings of the present study cannot be considered as evidence for the association between intraoperative BP fluctuation and POD. First of all, the study was observation and only 60 patients were included. Second, fluctuations in BP can be confounded by severity of overall illness or be a correlate of illness severity rather than a causal exposure. Patients with significant hemodynamic instability may also undergo more prolonged and complex surgeries, bleed more, need more vasopressors, require more cardiopulmonary bypass time or develop other complications that can independently increase the risk of delirium. Third, the current analysis was performed with a categorical classification of BP fluctuation instead of a continuous quantitative measurement. Thus, there is no way to rule out residual confounding.

The overall prevalence rate of postoperative cognitive dysfunction (PCD) in this study (35.0%) is also similar to the known burden of neurocognitive complications after cardiac surgery. Current data suggest that, despite this, cognitive dysfunction is relatively prevalent post-CABG, especially in the immediate postoperative period. The mechanisms are probably multifactorial, and may be similar to those in delirium such as cerebral hypoperfusion, microembolization, inflammation, impaired oxygen delivery, metabolic disturbances, and perioperative physiological instability. Importantly, delirium and postoperative cognitive dysfunction are not entirely separable events as delirium can be an acute expression of cerebral vulnerability, as well as, and perhaps more important, coexist with or contribute to subsequent cognitive dysfunction.

As a whole, Tables 1–3 show that POD occurred in this cardiac surgical population and that there were some clinically relevant characteristics associated with the presence of POD. There was a significant association between advanced age and POD, while diabetes and type of cardiac surgery did not show significant association with POD. Most importantly, significant intraoperative BP fluctuation was associated with a substantial increase in the observed rate of POD (27.8 percentage points with a crude risk ratio of ~1.83). These results could be extrapolated to other emerging evidence indicating that perioperative hemodynamic instability and BP variability could be important to postoperative neurologic outcomes.[20,21]

The results, however, must be taken with a pinch of salt due to the small sample size and the design that was used as an observation study. Also, because of the limited number of subjects, the reliability of the comparisons among subgroups is limited, especially in the VSD repair group (n = 2). More data would be provided by larger prospective studies that incorporated continuous measurement of IoBVP, a standardized definition of hypotension/hypertension, repeated assessments for delirium, and multivariable adjustment for age, sex, diabetes, type and duration of surgery, duration of cardiopulmonary bypass, transfusion, use of vasoactive medication, and other perioperative factors.

Clinically, the present results suggest that caution should be used in managing heart rates and blood pressures during surgery and that the systematic screening of delirium should be encouraged in cardiac surgical patients. Special attention might be given to older patients and patients with significant intraoperative BP fluctuations. However, no universal threshold should be used to guide management of BP as the autoregulatory range of the cerebral circulation is unique to each patient. Future studies should therefore aim to prevent absolute hypotension as well as to reduce excessive BP variability and, if feasible, have personalised targets for haemodynamics.

## CONCLUSION

Delirium following cardiac surgery is an important neurocognitive complication that is caused by the combined action of multiple physiological stressor and a predisposition of the patient. Of the current 60 cardiac surgical patients, 60.0% experienced substantial changes in the intraoperative BP. However, there was a statistically significant association between POD and BP fluctuations, as it was present in 61.1% of patients with BP fluctuations and 33.3% of patients without significant BP fluctuations (p=0.03). The other factors significantly associated with POD were advanced age and female sex, while diabetes mellitus and surgical procedure were not significant in this cohort.

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