TOPIC: Risk Factors and Outcomes for Postoperative Delirium in Post Cardiac Surgical Patients

AUTHOR: Allen N. Gustin, Jr., M.D., F.C.C.P.

Learning Objectives: After attending this session, each participant will be better able to do the following:

1. Describe the scope of delirium in the cardiac surgery population
2. Recognize modifiable and non-modifiable risk factors for delirium in cardiac surgery
3. List the effect of benzodiazepines on delirium and outcomes in the critically ill

Presentation Outline:

1. Introduction to Delirium:
   a. Definition of delirium
   b. Detection of delirium
   c. Problems with the delirium evaluation
2. DSM IV and CAM ICU criteria
3. Adult and Pediatric Studies
4. Delirium Outcomes
5. Delirium due to Cardiac Surgery
6. Risk factors for Postop Post Cardiac Surgery Delirium
   a. Cerebral oximetry
7. Prediction of Delirium
8. Prevention of Delirium
   a. Risperidone
9. Modifiable Risks for Delirium in the ICU
10. Benzodiazepines and Use in the ICU Patient Population

Introduction to Delirium:

Delirium is defined as an acute cognitive disorder presenting in patient where fluctuations in cognition, apathy, and non organized thinking. Delirium includes alterations in attention, cognition, consciousness, and perception; and is often associated with changes in sleep patterns. The main characteristic of delirium is inattention. It can also be termed intensive care unit (ICU) psychosis or ICU delirium. Delirium is categorized as either hyperactive or hypoactive. Hyperactive delirium puts the patient at greater risk of self-extubation, of accidental removal of life saving/invasive catheters, and of worsening patient ventilator synchrony. On the other hand, hypoactive delirium can result in a quiet but neglected patient given the decreased motion (hypoactive delirium suggests a worse prognosis). CAM ICU (Confusion Assessment Method of the ICU) is most
commonly used to evaluate the prevalence of delirium, though many studies will also use the DSM IV Criteria for Delirium.

Problems with delirium research in the perioperative period can be difficult. Multifactorial issues make it difficult to distinguish between emergence delirium from anesthesia and the other forms of delirium. One paper considered delirium after cardiac surgery to be quite distinct from other forms of delirium for the following reasons: 1. Different surgical populations have different medication profiles and require different anesthesia techniques (thus pharmacological triggers of delirium will vary depending on the surgery), 2. The use of cardiopulmonary bypass in cardiac surgeries requires special consideration since its use is associated with postoperative effects on neurotransmitter function and an increase in delirium, and 3. It is unknown if the pathophysiology of different postoperative deliria differs (research has shown that predictors of delirium appear to vary depending on the surgery type and the levels of various biomarkers for delirium).

Overall, postoperative post cardiac surgical delirium appears to be the result of a complex interplay of preexisting predisposing risk factors and peri/post operative risk factors. Preoperative cognitive dysfunction (reported to be 17.8% in cardiac surgery) had been identified as a major predisposing risk factor for delirium in some studies but has not been identified as a risk in others.

Confusion Assessment Method of the ICU (CAM ICU) and DSM IV Criteria for Delirium:

Regarding the existing delirium research, one of the two following methods is used for the detection of delirium in ICU patients: CAM ICU method and the DSM IV Criteria.

CAM ICU: Presented as a worksheet for healthcare providers to fill out. Four Features are included in the assessment.

**Feature 1: Acute Onset or Fluctuating Course.** Is the patient different than his/her baseline mental status? **OR** has the patient had any fluctuation in his/her mental status in the past 24 hours as evidenced by fluctuation on a sedation scale (RASS=Richmond Agitation Sedation Scale), GCS (Glasgow Coma Scale), or previous delirium assessment?

**Feature 2: Inattention.** This Feature uses the *Letters Attention Test.* Directions for the healthcare provider: Say to the patient, “I am going to read you a series of 10 letters. Whenever you hear the letter ‘A,’ indicate by squeezing my hand.” Read the letters from the following letter list in a normal tome 3 seconds apart: SAVEAHAART. Errors are counted when a patient fails to squeeze on a letter “A” and when the patients squeezes on any letter other than ‘A.”
**Feature 3: Altered Level of Consciousness.** Present if the Actual RASS (Richmond Agitation Sedation Score) is anything other than alert and calm (equates to a RASS = 0).

**Feature 4: Disorganized Thinking.** This feature uses both a series of yes/no questions AND a command. The yes/no questions include the following four questions: 1. Will a stone float on water? 2. Are there fish in the sea? 3. Does one pound weigh more than two pounds? 4. Can you use a hammer to pound a nail? Errors are counted when the patient incorrectly answers a question. The command includes the following: Say to the patient, “hold up this many fingers” (hold 2 fingers in front of the patient). “Now do the same thing with the other hand” An error is counted if patient is unable to complete the entire command.

Scoring for CAM ICU: 1 plus 2 and either 3 or 4 present = **CAM ICU positive**


A. Disturbance of consciousness (reduced clarity of awareness of the environment) with reduced ability to focus, sustain, or shift attention.
B. A change in cognition or the development of a perceptual disturbance that is not better accounted for by a pre-existing, established, or evolving dementia.
C. The disturbance developed over a short period of time (usually hours to days and tends to fluctuate during the course of the day.
D. There is evidence from the history, physical examination or laboratory findings that the disturbance is caused by the direct psychological consequences of a general medical condition.

**Studies Focusing on Delirium in Adults:** Predominately only adult research exists on the topic of post cardiac surgical delirium.

**Studies Focusing on Pediatrics:** No prospective, randomized, or cohort research studies looking at pediatric patients and postoperative delirium were identified.

**Delirium as it Applies to Patient Outcomes:**

Delirium in ICU patients in the postoperative period from cardiac surgery varies from 8.4% to 41.7%.(1) Delirium in ICU patients postoperatively has shown to increase ICU mortality, increase length of ICU stay, and increase ICU costs.(1,2,3) In patients who are post cardiac surgery, delirium can increase postoperative complications such as respiratory insufficiency, sternum instability, and need for
reoperation of the sternum.(1) In one study, delirium was present in 23.5% of postoperative cardiac surgical patients and the risk of delirium was higher in older patients, those who had cardiopulmonary bypass, those with atrial fibrillation, and those with a history of stroke (cerebrovascular accident).(1) The mean time on the mechanical ventilator for patients with delirium was more than in patients without delirium.(1) Increased length of stay in both the ICU and in the hospital has been seen in patients with postoperative cardiac surgical patients with delirium.(3) Patients with delirium in the ICU had increased rates of cognitive defects after discharge from the hospital.(3) Patients who had delirium post cardiac surgery had a mortality that was higher (than those without delirium) for one year after the ICU stay.(3)

Risk Factors for Delirium:

Older age (1,3,6,>60 in 7,>60 in 8,>65 in 9,>65 in 10)
History of CVA (1,3,7,10,11)
Prolonged mechanical ventilation (1,6,8,>24 hours in 10)
Atrial fibrillation (1,6,9,11)
Episodes of major depressive disorder (variable in 2,6,7)
Cardiopulmonary bypass (1,duration of CPB in 3)
Preoperative Cognitive impairment (6,7)
Diabetes (not in 1, yes in 9)
Hypertension (9,11)
Intraoperative fentanyl (2)
Intraoperative ketamine (2)
Preoperative antipsychotics (2)
Postoperative inotropes (2)
Lower MMSE (Mini Mental Status Exam) scores (3)
Emergency cardiac surgery (9)
Peripheral vascular disease (9)
Abnormal serum albumin (7)
Postop SIRS (3)
Use of intra aortic balloon pump (9)
Intraoperative hemofiltration (9)
Operation time > 3 hours (11)
Alcohol abuse (11)
Anemia (6)
Higher C Reactive Protein postop (3)
Infection after surgery (10)
Hematocrit < 30 (10)
Duration of cardiopulmonary bypass (8)
Preoperative use of an antipsychotic for one year (2)
Nicotine abuse (3)
Cerebral Oximetry for Delirium Risk for On-Pump Cardiac Surgery: (12)

A total of 231 patients were scheduled for elective cardiac surgery and enrolled into this study. ICU delirium was assessed by the CAM ICU criteria on the first three ICU days after cardiac surgery. ScO2 (cerebral oximetry) values were obtained on the day before surgery, immediately before surgery, and throughout the surgical procedure. Preoperative cognitive function, demographics, surgery related/intraoperative/postoperative physiological data were all registered. Patients with delirium had lower pre and intra-operative ScO2 readings, were older, had lower mental status examination scores, and lower preoperative hemoglobin levels. The binary regression identified older age, lower MMSE, neurological or psychiatric disease, and lower preoperative ScO2 as independent predictors of postoperative delirium. Thus, a low preoperative ScO2 is associated with postoperative delirium after on pump cardiac surgery.

Prevention of Delirium:

A great deal of emphasis has been placed on trying to determine if delirium can be prevented. Efforts to evaluate the effects of perioperative medications on the incidence of delirium has been receiving the greatest focus. (2) Given the changes in/excess of neurotransmitters like dopamine, norepinephrine, and epinephrine in the perioperative state, attention is being focused on pharmacology as a means of modifying the risks for postoperative delirium. (2) Attention has been paid to drugs that have anticholinergic properties (digoxin, furosemide, or nefedipine) that might play a role in delirium. (2) Also, selective serotonin reuptake inhibitors (SSRIs), antipsychotics, and benzodiazepines may also play important contributors to delirium etiology though neurotransmitter pathways. (2) One drug, postoperative risperidone (taken upon awakening) (2) has shown to help in the prevention of postoperative post cardiac surgical delirium.

**Preoperative drug administration.** Mixed results on drug effect on postoperative delirium were seen with the following drugs: statins, anticholinergic agents, antidepressants, selective serotonin reuptake inhibitors (SSRI), and benzodiazepines. No effect on postoperative delirium was seen for the use of cholinesterase inhibitors, opioids, diuretics, calcium channel blockers, Beta blockers, ACE inhibitors, angiotensin receptor blockers, Nitrates, or benzodiazepines. Increased risk of postoperative delirium was seen when antipsychotics were used in a patient in the weeks that led up to the date of surgery. (2)

**Intraoperative drug administration.** No effect on postoperative delirium was seen with intraoperative diazepam. Mixed results have been seen with fentanyl. Possible decreased incidence of postoperative delirium has been seen with ketamine. (2)
Postoperative administration of these drugs: Mixed results were seen for effects on postoperative delirium with the use of dexmedetomidine. No effect on postoperative delirium was seen with the use of morphine or opioids. Increased risk of postoperative delirium was seen with the use of inotropes postoperatively.(2)

Prophylactic regimens: Decreased incidence of postoperative delirium with the immediate postoperative use of risperidone.(4)

Prevention of Delirium postoperatively with Risperidone:(4)

Randomized double blind placebo controlled study of 126 patients after cardiopulmonary bypass. Patients were to receive either 1 mg of risperidone (sublingual administration) or placebo when they regained consciousness in the ICU. Patients were assessed for delirium using the CAM ICU. The incidence of postoperative delirium was 11% percent in the risperidone group versus 31% in the control group (P = 0.009). Many other perioperative factors were associated with postop delirium but there was no statistical difference between the two groups regarding these factors. Final outcome: one dose of risperidone administered relatively soon after cardiac surgery reduced the incidence of postoperative delirium.

Prediction of Delirium: One study was able to predict postoperative post cardiac surgical delirium using the combination of age, Mini Mental Status Exam score, and length of cardiopulmonary bypass with a sensitivity of 71.2% and a specificity of 26%.(3)

Dexmedetomidine Versus Midazolam for Sedation in ICU Patients: (13)

ICU Study: Randomized prospective double blind trial in 5 countries for two years. Sedation for ICU patients. RASS and CAM ICU were used for assessment of delirium. RASS was targeted to -2 to 1. Primary outcome was the target RASS range. Other outcomes: duration of mechanical ventilation, ICU length of stay, and adverse events.

Results: No difference between both drugs regarding the time within the target RASS range. The prevalence of delirium during treatment was 54% in the dexmedetomidine group versus 76.% in the midazolam treated patients. Time to extubation after the procedure was 1.9 days shorter in the dexmedetomidine treated patients and the ICU stay was similar between the two groups. Dexmedetomidine treated patients were more likely to develop bradycardia with a non-significant increased need to treat the bradycardia. Overall, no difference between dexmedetomidine and midazolam were found as related to time at
targeted sedation level in mechanically ventilated ICU patients. At comparable sedation levels, dexmedetomidine treated patients spent less time on the ventilator, experienced less delirium, and developed less tachycardia/hypertension.

**Lorazepam is an Independent Risk Factor for Determining to Delirium in Intensive Care Unit Patients** (14)

This was a cohort study in order to investigate whether sedative and analgesic mediations independently increased the probability of daily transition to delirium. A total of 198 mechanically ventilated patients were enrolled to determine the probability of delirium as a function of sedative and analgesic dose during a drug's administration during the previous 24 hours. Lorazepam was an independent risk factor for daily transition to delirium (OR 1.2; P = 0.003); whereas fentanyl, morphine, and propofol were associated with higher but not statistically significant odds ratios. Increasing age and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores were also independent predictors of transitioning to delirium. Lorazepam administration is an important and potentially modifiable risk factor for transitioning into delirium even after adjusting for relevant covariates.

**Modifiable Risk Factors in the Cardiac Surgical ICU: (15)**

This is a prospective observational study involving 200 patients in a cardiovascular ICU. Patients include both postoperative cardiac surgical and cardiology ICU patients. Delirium occurred in 26% of the cardiology and cardiac surgical patients. Almost 92% of the patients with delirium had the hypoactive form. Patients were prone to delirium when exposed to benzodiazepines (OR 2.6, p=0.02) or when restraints were used (OR 2.9, p<0.01) during the stay in the cardiac surgical ICU. Hemodynamic status was not associated with delirium in this study. Thus, benzodiazepine use and use of restraints were the only two modifiable risk factors identified for reducing the incidence of postoperative post cardiac surgical delirium.

**Conclusions:**

Few modifiable risk factors have been identified that could reduce the likelihood of postoperative post cardiac surgical ICU delirium. One should consider the avoidance of benzodiazepines for sedation, the avoidance of restraints in the ICU after cardiac surgery, the use of risperidone in the postoperative period, and control of atrial fibrillation as a means of reducing the likelihood of delirium after cardiac surgery. (1,4,6,9,11,15) No single prediction tool for delirium is going to be 100%. However, knowledge of all risk factors will be there to help identify patients at risk. (3)
References: