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DELIRIUM POST CARDIAC SURGERY: REVIEW ON EPIDEMIOLOGY AND ASSOCIATED RISK FACTORS

Abla M. Habeeb-Allah[1] & Jafar Alasad[2]

[1]Research Scholar, Princess Muna College of Nursing, Amman, Jordan

[2]Professor, School of Nursing /University of Jordan, Amman, Jordan

ABSTRACT

Background: *Delirium is a multifaceted condition in which the exact pathophysiology is still unknown. There are enormous risk factors associated with the development of delirium. Post cardiac surgery delirium is prevalent.*

Aim: *This literature review is aimed to identify the incidence and associated risk factors of delirium among the population of post cardiac surgery adult patients.*

Methods: ***L****iterature search was carried out on CINAHL, MEDLINE, Google Scholar, Ovid, and Science Direct. The searching timeframe has been limited between the years 2012 and 2017.*

Findings: ***T****hirteen studies were included in the final review. Incidence of delirium post cardiac surgery varied from 4.1% up to 68%. Post cardiac surgery delirium associated risk factors are categorized as preoperative, intraoperative, and post operative risk factors. Among the most frequently associated factors are advancement of age, stroke, hypertension, atrial fibrillation, history of diabetes mellitus, prolonged Cardio Pulmonary Bypass (CPB) time, time spent on mechanical ventilation, length of ICU stay, and transfusion of blood and it is products.*

Conclusion: *There is a gap in the estimated incidence of delirium post cardiac surgery patients in addition to varied identified risk factors, because of the use of different diagnostic tools and protocols for delirium assessment. There is a need for a unified, standardized tool for delirium assessment among this population.*

KEYWORDS: *Delirium, Post Operative Delirium, Prevalence, Incidence, Risk factors, Cardiac Surgery, and Intensive Care Units*

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INTRODUCTION

Delirium is an acute, multifaceted, neuropsychiatric syndrome that is characterized by acute onset and fluctuating course, inattention, impaired consciousness, and disordered cognition (American Psychiatric Association, 2013). Delirium is a condition that is widely known to be associated with increased morbidity and mortality rate as well as increased health care costs (O'Neal and Shaw, 2016). Delirium affects about 20% of general hospital inpatients (Bellelli, et al, 2016; Ryan, et al., 2013). In Intensive Care Units (ICU), around 32% (Salluh, et al., 2015) and up to 80% of admitted patients could develop delirium (Vasilevskis, et al., 2012). Post Operative Delirium (POD) affects about 87% of

surgical patients (McDaniel and Brudney, 2012). Delirium approximately affects half of the post cardiac surgery patients (Brown, 2014).

Background

Delirium is associated with various precipitating and predisposing risk factors, including age, preexisting cognitive impairment, co-morbidities, complicated surgeries, physical stress, and infections (Grover and Kate, 2012). Among the risk factors of post cardiac surgery delirium are advanced age, preexisting stroke, hypertension, atrial fibrillation, diabetes mellitus, smoking, alcohol intake, obesity, Cardio Pulmonary Bypass (CPB) time, time of mechanical ventilation, ICU stay, blood transfusion, pain, dehydration, low cardiac output, hypoxia, immobilization, postoperative medication, and sedation (O'Neal and Shaw, 2016; Cropsey, et al., 2015; Lin, et al., 2012). There is a strong association between risk factors and development of POD. The risk to develop POD is as low as 9% when patients have no risk factors. This risk increased to be 23% with one or two risk factors, and it became as high as 83% with three or more risk factors (Dormer, 2015). Fortunately, some of delirium related risk factors are preventable (O'Neal and Shaw, 2016).

Delirium Definition

The American Psychiatric Association's Diagnostic and Statistical Manual, 5th edition (DSM-V) identifies five key criteria for the diagnosis of delirium: a disturbance in attention and awareness; the disturbance is acute and represents changes from baseline awareness and attention and develops over a short period of time and could fluctuate during the course of the day; a disturbance in cognition occurs (memory deficit, disorientation, language, or perception); these disturbances are not explained by another neurocognitive disorder and do not occur during a state of reduced level of arousal including coma; and there is evidence to suggest that the disturbance is caused by a medical condition, substance intoxication or withdrawal, side effect of a medication, or due to multiple etiologies (American Psychiatric Association, 2013).

Pathogenesis

Delirium is a complex condition in which it is exact mechanism or cause is not discovered yet and it is pathophysiology is poorly understood (Francis and Young, 2014; Inouye, et al., 2014). Instead, existing evidence yields a combination of several factors and mechanisms that leads to acute confusional state of the brain. Among these mechanisms and biological factors are neurotransmitters, inflammation, physiological stressors, metabolic disorders, electrolyte disturbances, and genetic factors (Inouye, et al., 2014). Three main types of neurotransmitters are responsible for the development of delirium: acetylcholine, dopamine, and Gabba Aminobutyric Acid (GABA). Delirium is thought to be developed as a result of the imbalance of these neurotransmitters which lead to unpredictable and inconsistent activity of brain neurotransmission. Therefore, any disease, intervention, medication, or model of care could affect these neurotransmission is predisposing to the development of delirium (Perrin and MacLeod, 2018).

Diagnosis

Delirium is a clinical diagnosis that is poorly recognized at the clinical settings (Inouye, et al., 2014). Unfortunately, more than seventy percent of delirium cases are not recognized (Francis and Young, 2014). Proper identification of delirium necessitates knowledge of the previous cognitive state of the patient. Information about previous cognitive state of patients can be obtained from nurses, care givers, as well as patients' families. Psychiatric

evaluation of delirium based on the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria is the golden standard in delirium diagnosis (Whitlock, et al., 2011). However, several clinical instruments that can be used by non-psychiatric clinicians were established and tested for their abilities to detect delirium in clinical settings. The Confusion Assessment Method (CAM) is a simple tool that is highly recommended in different medical and surgical settings. This is because CAM is proved to be a reliable and valid assessment tool; it is easy to be administered by non-psychiatric clinicians in less than five minutes, and because it can be used in different settings including emergency rooms and long-term settings (Francis and Young, 2014). The Confusion Assessment Method for Intensive Care Unit (CAM-ICU) is a modified version of CAM that has high psychomotor properties and can be used in mechanically ventilated patients who are unable to communicate verbally (Ely, 2016).

Methods

The search strategy for this review was guided by the review aim. The following databases were searched to retrieve related literature: the Cumulative Index to Nursing and Allied Health Literature (CINAHL) via Ebesco, MEDLINE via PubMed, Ovid, Science Direct, and Google Scholar. Studies presented in English for the period between 2012 and 2017 were included. Search terms used were: delirium, post operative delirium, prevalence, incidence, risk factors, cardiac surgery, intensive care units, and delirium outcomes. Thirteen studies were included in the final review. Table (1) displays a summary of reviewed studies of post cardiac surgery delirium.

Epidemiology

Application of standardized delirium assessment measures increases the efforts toward knowing of clinical epidemiology of delirium (Francis and Young, 2014). The main reason of such studies is to provide best understanding of this complicated phenomenon which in turns will enhance prevention and management of delirium. Delirium among hospitalized patients affects nearly 30%; this risk increased to be greater than 50% among older surgical patients and higher figures are associated with more complicated surgical procedures such as cardiac surgeries (Francis and Young, 2014). Post operative delirium among cardiac surgery patients is a prevalent complication. The incidence estimates of delirium among post cardiac patients are widely varied from 3% to 70% (Brown, 2014) and from 11.5% to 52% in other studies (Lin, et al., 2012). This variation is due to different methods and assessment protocols followed to diagnose delirium and a lack of consensus of standardized tool that can assess delirium and it is severity.

Incidence of delirium post cardiac surgery patients in this review varied from 4.1% (Krzych, et al., 2014) up to 68% (Fallahpoor, et al., 2016). Variation of these estimates is related to different factors including patients' age, type of cardiac surgery, and assessment methods used to diagnose delirium. Incidence of delirium increased in the population of patients with advanced age. Type of the cardiac surgery also contributes to this variation since delirium is more frequent post valve replacement surgery in comparison with bypass surgery (Sockalingam, et al., 2005). Generally, lower incidence of post cardiac surgery delirium ranged from as low as 4.1% to 30% (Giuseffi, et al., 2017; Kumar, et al., 2017; Mufti and Hirsch, 2017; Rudiger, et al., 2016; Andrejaitiene, et al., 2015; Cropsey, et al., 2015; Mangusan et al, 2015; Krzych, et al., 2014; Jodati, et al., 2013; Norkienė, et al., 2013; Shadvar, et al., 2013; Taipale, et al., 2012) and higher incidence reported from greater than 30% to be as high as 68% (Cereghetti, et al., 2017; Fallahpoor, et al., 2016; Breu, et al., 2015; Zhang, et al., 2015; Bakker, et al., 2012).

Risk Factors

The etiology of delirium is multifactorial although one factor can lead to the development of delirium such as alcohol withdrawal or substance abuse (Inouye, et al., 2014). There is a well known group of risk factors associated with delirium established by research. Inouye and Charpentier (1996) developed a model in which delirium related risk factors are displayed as predisposing and precipitating factors (Figure 1).

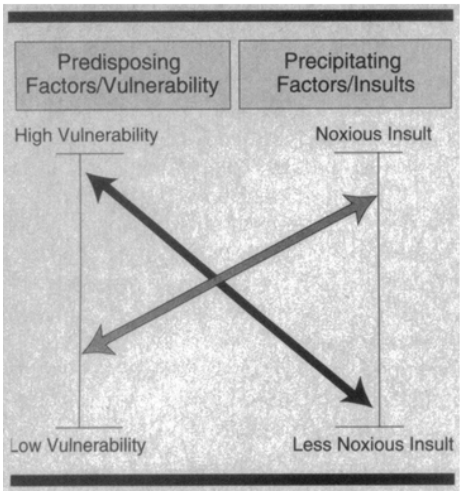

Figure 1: The Multifactorial Model of Delirium (Inouye and Charpentier, 1996)

Predisposing factors are those which make patient vulnerable to develop delirium such as age, being male, visual impairment, hearing impairment, history of dementia, preexisting depression, and co-morbidities. Precipitating factors are those which considered as subsequent insults that trigger delirium such as complicated surgeries, physical stress, and infections. Delirium developed as a result of the interrelationship of patients predisposing and precipitating factors (Martins and Fernandes, 2012). Effects of these factors is accumulative which means the more factors exist, the greater the risk of delirium (Clegg, et al., 2012).

Delirium associated risk factors among patients post cardiac surgery as any type of post operative delirium are mainly classified as preoperative, intraoperative, and postoperative factors. Each one of risk factors could be modifiable or non-modifiable; hence, working on modifiable risk factors is central to prevent the occurrence of delirium. In some instance, presence of one or more of certain post cardiac surgery risk factors such as depression, cognitive impairment or history of stroke is able to double or even triple the risk of occurrence of post operative delirium (Clegg, et al., 2012). Among the most common preoperative risk factors for delirium post cardiac surgery are: advance age, male gender, cerebral ischemia and stroke or transient ischemic attack, cognitive impairment, low cardiac output, preoperative anemia, dehydration, atrial fibrillation, smoking, alcohol consumption, addiction, electrolyte imbalance, low serum albumin, malnutrition, low preoperative cerebral oxygenation, and medication used by patient before surgery (Indja, et al., 2017; O'Neal and Shaw, 2016; Cropsey, et al., 2015; Lin, et al., 2012).

Intraoperative risk factors includes Cardio Pulmonary Bypass (CPB) time that affects brain perfusion and oxygenation, intra-operative medication, type and amount of anesthetic agents, hypovolemia, type of surgery (Coronary Artery Bypass Graft (CABG), valve repair and/or replacement, aortic aneurysm repair), combination of more than one surgical intervention (e.g. aortic coronary bypass graft and valve replacement), time of surgery, hypoxemia,

and low Mean Arterial Pressure (MAP) (O'Neal and Shaw, 2016; Cropsey, et al., 2015). Postoperative factors involve post operative pain, sleep deprivation, unfamiliarity with the ICU and hospital environment, transfusion of blood and it is products, hypoxia, low cardiac output, time of mechanical ventilation, ICU and hospital length of stay, restrains, immobilization, pharmacology used and combination of more than two medications, postoperative sedation, urinary catheters, hypotension, increase inflammatory markers, and elevated cortisol levels (Cropsey, et al., 2015; Lin, et al., 2012).

Factors associated with post cardiac surgery delirium risk in this review are presented in table (1). The most reported predisposing factor (vulnerability) is advance age followed equally by preexisting stroke, hypertension and atrial fibrillation then by history of diabetes mellitus. Other but less frequent predisposing factors include male gender and other co-morbidities as smoking, alcohol intake, and obesity. Regarding the precipitating (insult) factors, the Cardio Pulmonary Bypass (CPB) time and time of mechanical ventilation are the most reported factors. Time of surgery also is commonly mentioned but it implicitly includes CPB time and other interventions and complication that could evolve during the surgery. Other frequently reported precipitating factors are ICU stay and transfusion of blood and it is products.

CONCLUSIONS

The incidence of delirium is thought to be increased in the future because of the expected demographic change of the increased population age. The need for more studies that clarify POD particularly post cardiac surgery is strongly recommended. Moreover, further research is required to better identify the best strategy in managing delirium after cardiac surgery.

Identification of incidence and associated risk factors of delirium promote the delivery of safe and quality health care which consequently decreases morbidity, mortality, health care costs, and improves patients' outcomes as well. Awareness of post cardiac surgery delirium incidence and risk factors is crucial in the improvement of delirium outcomes by early detection and prevention. Lack of adherence of assessment protocols for delirium in this population make incidence of delirium clinically under-recognized. Early identification of patients at risk for delirium post cardiac surgery is essential to enable implementation of modifiable risk factors' interventions that prevent delirium.

Table 1: Summary of Studies Investigating Post Cardiac Surgery Delirium (2012 – 2017)

Authors & Year	Incidence	Sample Size	Assessment Tool	Associated Risk Factors
Andrejaitiene, et al., (2015)	28%	323 patients	Intensive Care Delirium Screening Checklist, CAM-ICU, RASS, Nursing Delirium Screening Scale	Age, History of stroke, dose of Intraoperative use of thiopental, length of hospital stay before surgery, and re-intubation.
Bakker, et al.,(2012)	31%	201 Patients aged > 70 years	CAM-ICU	Preoperative Mini-Mental State Examination score, preoperative creatinine level, and CPB time.
Fallahpoor, et al., (2016)	- 68% without intervention - 38% with intervention	100 patients	CAM-ICU	Age, Co-morbidity (DM, obesity, Hypertension, hyperthyroidism, smoking, addiction, alcohol intake), AF rhythm, preoperative narcotic, CPB time, post operative pain, hypoxia, electrolyte imbalance, blood transfusion.
Authors & Year	**Incidence**	**Sample Size**	**Assessment Tool**	**Associated Risk Factors**
Giuseffi, et al., (2017)	21%	121 patients	CAM-ICU	Age, type of surgery (transcatheter Vs. surgical aortic valce replacement)
Jodati, et al.,(2013)	4.9 %	329 patients	Minnesota Multiphasic Personality Inventory	AF, Lung disease, Hypertension, CPB time, ICU stay, Mechanical ventilation time, and being female.
Krzych, et al.,(2014)	4.1%	5,781 Patients	Criteria of the Diagnostic and Statistical Manual of Mental Disorders IV edition (DSM-IV)	Age, CPB time, history of CAD, DM, hypertension, and COPD.
Kumar, et al.,(2017)	17.5%	120 patients	CAM-ICU	History of hypertension, stroke as a result of carotid artery disease, use of non-invasive ventilation, length of ICU Stay, poor post operative pain control.
Authors & Year	**Incidence**	**Sample Size**	**Assessment Tool**	**Associated Risk Factors**
Mufti and Hirsch(2017)	11.4% Only hyperactive delirium	5584 patients	CAM-ICU confirmed by psychiatrist assessment and mini-mental test	Age, male gender, history of stroke, procedure other than isolated Coronary Arteries Bypass Surgery, transfusion of blood products, time of mechanical ventilation, and length of stay in ICU
Norkienė, et al.,(2013)	13.3%	87 patients	Intensive Care Delirium Screening Checklist	Post operative transfusion of blood product, low cardiac output, time of mechanical ventilation, length of ICU stay, and duration of surgery.
Rudiger, et al.,(2016)	26%	194 patients	Intensive Care Delirium Screening Checklist Or CAM-ICU	Only Intraoperative variables are included: time of CPB, low mean arterial Pressure, low temperature, low hemoglobin level, high nor-adrenaline support, and transfusion of platelets.
Shadvar, et al.,(2013)	23.5%	200 patients	CAM-ICU	Age, CPB time, Stroke, AF, time of mechanical ventilation
Authors & Year	**Incidence**	**Sample Size**	**Assessment Tool**	**Associated Risk Factors**
Taipale, et al.,(2012)	22.1%	122 patients	CAM-ICU	Use of Midazolam, Age, and history of peripheral vascular disease
Zhang, et al.,(2015)	30.52%	249 patients	CAM-ICU	AF, elevated European system for cardiac operative risk evaluation, cognitive impairment, surgery duration, postoperative poor quality of sleep, and electrolyte disturbance.

CAM-ICU: Cognitive Assessment Method for Intensive Care Unit, ICU: Intensive Care Unit, CPB: Cardiopulmonary Bypass, AF: Atrial Fibrillation, DM: Diabetes Mellitus, COPD: Chronic Obstructive Pulmonary Disease.

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