An-Najah National University

Faculty of Graduate Studies

Intraoperative pathophysiological changes and therapeutic interventions in patients undergoing on-pump cardiac surgery may be risk factors for the development of postoperative Delirium. Observational Study

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Dedication

بسم الله الرحمن الرحيم

(قل إعملوا فسيرى الله عملكم ورسوله والمؤمنون)

صدق الله العظيم

إلهي لايطيب الليل إلا بشكرك ولايطيب النهار إلى بطاعتك .. ولاتطيب اللحظات إلا بذكرك .. ولا تطيب الآخرة إلا بعفوك .. ولا تطيب الجنة إلا برؤيتك

الله جل جلاله

إلى من بلغ الرسالة وأدى الأمانة .. ونصح الأمة .. إلى نبي الرحمة ونور العالمين ..

سيدنا محمد صلى الله عليه وسلم

إلى من كلله الله بالهيبة والوقار .. إلى من علمني العطاء بدون انتظار .. إلى من أحمل أسمه بكل افتخار .. أرجو من الله أن يمد في عمرك لترى ثماراً قد حان قطافها بعد طول انتظار وستبقى كلماتك نجوم أهتدي بها اليوم وفي الغد وإلى الأبد

(والدي العزيز)

إلى ملاكي في الحياة .. إلى معنى الحب وإلى معنى الحنان والتفاني .. إلى بسمة الحياة وسر الوجود

إلى من كان دعائها سر نجاحي وحنانها بلسم جراحي إلى أغلى الحبايب

أمي الحبيبة

إلى من بها أكبر وعليه أعتمد .. إلى شمعة متقدة تنير ظلمة حياتي ..

إلى من بوجودها أكتسب قوة ومحبة لا حدود لها ..

إلى من عرفت معها معنى الحياة

أختي .....

إلى أخي ورفيق دربي وهذه الحياة بدونك لاشيء معك أكون أنا وبدونك أكون مثل أي شيء .. في نهاية مشواري أريد أن أشكر على مواقفك النبيلة إلى من تطلعت لنجاحي بنظرات الأمل

أخي .....

إلى الأخوة الذين لم تلدهم أمي .. إلى من تحلو بالإخاء وتميزو بالوفاء والعطاء إلى ينابيع الصدق الصافي إلى من معهم سعدت، وبرفقتهم في دروب الحياة الحلوة والحزينة سرت إلى من كانوا معي على طريق النجاح والخير

إلى من عرفت كيف أجدهم وعلموني أن لا أضيعهم

أصدقائي .....

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الإقرار

أنا الموقع أدناه مقدم الرسالة التي تحمل العنوان:

Intraoperative pathophysiological changes and therapeutic interventions in patients undergoing on-pump cardiac surgery may be risk factors for the development of postoperative Delirium. Observational Study

أقر بأن ما اشتملت عليه هذه الرسالة إنما هي نتاج جهدي الخاص، باستثناء ما تمت الإشارة إليه حيثما ورد، وأن هذه الرسالة ككل، أو أي جزء منها لم يُقدم لنيل أية درجة أو لقب علمي أو بحثي لدى أي مؤسسة تعليمية أو بحثية أخرى.

Declaration

The work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

Student's Name: **اسم الطالب:**

Signature: **التوقيع:**

Date: **التاريخ:**

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Intraoperative pathophysiological changes and therapeutic interventions in patients undergoing on-pump cardiac surgery may be risk factors for the development of postoperative Delirium.

Observational Study

By

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Abstract

Introduction: Delirium after cardiac surgery is a common complication in cardiovascular intensive care units. Estimated incidence rates are approximately 2% to 72%. Delirium is an acute organic syndrome characterized by inattention, disorientation, along with global cognitive impairment and disturbance in consciousness. Postoperative delirium is typically characterized by a varying rate and can be associated with either increased or decreased psychomotor activity. Delirium after cardiac surgery to be quite distinct from other forms of delirium for the following reasons: Different surgical Populations have different medication profiles, require different anesthesia techniques thus pharmacological triggers of delirium will vary depending on the surgery, the use of cardio-pulmonary bypass in cardiac surgeries requires special consideration since its use is associated with postoperative effects on neurotransmitter function and an increase in delirium. Research has shown that predictors of delirium appear vary depending on the surgery type and the levels of various biomarkers for delirium. Identification of risk factors of delirium is important for positive postoperative outcomes.

Aim: The aims of this study are to investigate whether intra-operative events and therapeutic interventions affect the risk of postoperative delirium in patients undergoing cardiac surgery in the ICU and to determine the incidence of and risk factors for delirium in patients undergoing cardiac surgery.

Material and methods: A descriptive analytical study design used; study performed at cardiac surgery units at three hospitals in Palestine. Sixty patients who underwent elective cardiac surgery are subsequently admitted to cardiac surgical ICU are enrolled into this study. A detailed clinical report form was created to collect pertinent data in order to determine the effect of pre-operative, intraoperative and postoperative variables on delirium. All subjects are screened for delirium using the RASS and CAM‑ICU test once daily, and all those who tested positive were thereafter designated as cases and the other subjects are deemed controls.

Results: The percentage of patients who developed delirium right after the operation were 75.9% (41/54) of the targeted sample, the percentage continued to drop until it reached 3.7% (2 patients) in the second and third day. No relation could be detected between delirium and the demographic variables (education, smoking status, gender, marital status and age) and no relation could be detected between delirium and the pre-operative factors. Intraoperative, total amount of midazolam/mg in control group 3.31±0.398 compared to 2.41±.135 in delirium group, p= .051, (95% confidence level) and the result shows that those who did not suffer from delirium postoperative have had higher amount of midazolam. There was a significant difference at (90% confidence level) in the total amount of morphine/mg in control group

(no delirium) 8.85±1.04 compared to delirium group 7.93±.45 (p= .085), those who received more morphine intra-operatively where more likely not to develop delirium after the surgery. The variable with significant relation to delirium was the use of atropine (90% confidence level) as those who seemed to use more atropine were significantly less likely to develop delirium, as in control group (not delirium) 3 (23.1%) patients received atropine compared to delirium group 1 (2.4%), p= 0.062. Regarding temperature **(**95% confidence level) those patients who had low grade or high temperature 19(46.3) in delirium group compared to 0(0%) in the control group (p= 0.01) were significantly more likely to develop delirium. This result indicates that low grade or high temperature postoperative is a precipitating factor for delirium. Postoperatively, bolus doses of morphine/mg (95% confidence level) as in the control (not delirium) M(SD) .00±.000 compared to 1.17±.308 in the delirium group, p= (0.001) those patients who received morphine where significantly more likely to develop delirium postoperatively. Regarding the sequential organ failure assessment score (SOFA) (90% confidence level) as those patients who scored higher SOFA in the delirium group 5.56±.191were more likely to develop delirium compared with control group (not delirium) 4.85±.390, (p= 0.083). This result indicates that higher SOFA was a precipitating factor for delirium. Hyperactive type of delirium was seen in 22/41 patients (54.7%) while 11/41 patients (25.9%) had hypoactive delirium and 6/41 (13%) patients had mixed delirium.

Conclusion: A compelling percentage of cardiac surgical patients encountered delirium in ICU, broadly in its hyperactive form. Few modifiable risk factors have been determined that could lower the probability of post cardiac surgical ICU delirium. One should contemplate the use of midazolam, morphine and atropine intra-operative as protective drugs for postoperative delirium. Low and high grade fever, postoperative morphine usage and augmenting of SOFA score are precipitating factors for postoperative delirium.

Key words: Cardiac surgery; Delirium; CAM-ICU; Cardiac intensive care unit; Risk factors

Chapter One
Introduction

Introduction

Delirium is a prudent problem in cardiac surgery (Reade, et al., 2014). The occurrence of delirium endure to increase among cardiac surgery patients (Weinhouse, et al., 2006). The occurrence of postoperative delirium alter between 2% and 72% based on the type of surgery executed (Sockalingam, et al. 2005). The large variation is analogous to the definitions, the alterations in the diagnostic tools adopted and the different populations studied.

Delirium is an accompaniment of amended consciousness with simple aberration of thoughts. The pathophysiology of this complication is not sunny, but recognition of risk factors is crucial for positive results after surgery. Delirium is a serious side effect that is often not perceived by health care workers. Extensively, delirium can be interfered with in an approximated one-third of cases with simple non-pharmacological interventions accomplished by devoted healthcare professionals (Augoustites, et al., 2010).

Risk factors for delirium were newly summarized for ICU patients primarily and for patients who underwent cardiac surgery in particular. Solid evidence was reported for the subsequent risk factors: advanced age, cerebrovascular disease, psychiatric impairment and cognitive dysfunction, type of surgery, and peri-operative red blood cell (RBC) transfusions.

Other intraoperative variables, such as duration of cardiac bypass (CPB) or intraoperative transfusion of platelets, were incomparable or not yet considered (Kogan A, et al., 2003). Hypothermia upon entrance into the recovery room has also been expressed to be a risk factor for hypoactive onset (Xara, et al, 2016).

Delirium does not have a sole cause, but is better interpreted as having a multifactorial etiology. Different theories have been suggested regarding the progress of delirium by different mechanisms along with perioperative cerebral hypoperfusion (i.e. relative oxygen dependence) (Van Eijk, and Slooter, 2010), along with the result of overall physiological stress, amended neurotransmitter grades, neuronal aging, inflammatory cytokine dispense, and disruption in intra-neuronal signal transduction (i.e. intrusion with other messenger systems) has also been illustrated. Delirium is expected to be the result of reciprocal action between two or more of these aptitude mechanisms. This pathophysiological ramification of delirium devotes to its high prevalence in the context of cardiac surgery. Delirium as a problem of cardiac surgery was first described in the first few years after the commencement of modem vascular surgery in 1953.

Some medications have been shown to be combine with delirium, principally, these drugs with psychoactive potential such as benzodiazepines, corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDS), opiates and chemotherapeutic agents have been shown to be risk factors in delirium (Gaudreauj, et al., 2005).

Medicines with anticholinergic potential can also advance to delirium. A formerly mentioned relationship between serum anticholinergic activity **(**SAA) which indicates a drug's anticholinergic potential) and the development of delirium has been determined (Tune, et al., 1993).

Cardiac surgery patients who reacquire in the ICU are often concerned by amended sleep wake cycles, resulting in deep sleep deprivation. In the ICU, the average sleep time has been described to be as low as 2 hours over a 24-hour period. It has been hypothesized that sleep deprivation in critically ill can induce emotional distress, as well as devote to neurocognitive dysfunction, diminished immune function, lengthening of mechanical ventilation, and ICU delirium (Tune , et al., 1993). Thus, delirium in the patient after cardiac surgery may ensue as a result of amended sleep-wake cycles and its associated sleep deprivation, during cardiac surgery, the patient goes through trauma to which the body reacts by activating a "systemic inflammatory response". This can also enhance the risk of developing delirium. The inflammatory counter is more pronounced with a larger primary defamation. Therefore, cardiac surgery has a very conspicuous inflammatory response as a response to excess blood loss and transfusions, counting tissue trauma, ischemia and reperfusion of the myocardium, use of cardio-pulmonary bypass (CPB) and other causes (Weinhouse & Schwab, 2006).

Delirium after cardiac surgery to be comprehensively different from other modes of delirium for the following reasons: diverse surgical populations have various medication profiles and crave alternative anesthetic techniques, so pharmacological triggers of delirium will differ build upon the surgery, the usage of cardiac-pulmonary bypass in cardiac surgery craves exclusive attention since its use is combined with postoperative effects on neurotransmitter function and an increase in delirium, and it is unrecognized whether the pathophysiology of different postoperative delirium differs. Research has demonstrated that predictors of delirium alter based on the type of surgery and the levels of different biomarkers for delirium. Determining risk factors is important for positive results after surgery.

Aim of the study

The aims of this study are to investigate whether intra-operative events and therapeutic interventions affect the risk of postoperative delirium in patients undergoing cardiac surgery in the ICU and to determine the incidence of and risk factors for delirium in patients undergoing cardiac surgery.

Main Objectives

To determine if the incidences of intraoperative events of cardiac surgery are risk factors for the development of delirium in ICU.

Secondary objectives

- To investigate whether intra-operative therapeutic interventions affect the risk of postoperative delirium in patients undergoing cardiac surgery in the ICU
- To determine the incidence of delirium in patients undergoing cardiac surgery.
- To determine the risk factors for delirium in patients undergoing cardiac surgery.

Hypotheses

- There is a significant association at 0.10 level related to intra-operative pathophysiological alterations and postoperative delirium in cardiac surgery ICU patients.
- There is a significant association at 0.10 level related to intra-operative therapeutic interventions and postoperative delirium in cardiac surgery ICU patients.

Statement of the problem

Cardiac surgery patients are contemplated to have a heightened risk of developing delirium compared to other surgical patients. The occurrence of delirium after cardiac surgery has been expressed alter between various institutions, it is one of the most upsetting and common results of such surgery. Even with such a high incidence, delirium is often undiagnosed and thus many patients are sent home without complete settlement of symptoms (Maldonado, 2009). Delirium is mediated to be an independent risk factor for long-term hospital stay and 6-month mortality (Maldonado, 2008). Further, postoperative delirium has significant financial ramifications, which have been shown to be combined with 39% higher intensive care units and 31% higher hospital costs (Milbrandt, et al., 2004). Accordingly, investigate even if intraoperative changes and therapeutic interventions affect the risk of postoperative delirium in patients undergoing cardiac surgery in ICU patients and wind up the prevalence and risk factors for delirium in patients undergoing cardiac surgery. An improved perception of these topics can set up better recognition of patients at risk and the design of intervention studies. Efforts to prevent delirium can have a significant influence on the health care system and patient outcomes and are an area of heightened interest in research.

The significance of the study

Delirium is a prevailing and life-threatening condition of intensive care (Christensen, 2013). Even with expanded research, postoperative delirium is a problem that attends to long-term hospitalization, elevated costs and raised mortality (Arenson et al., 2013; Norkiené et al., 2013). There are a lot of predisposing factors for postoperative delirium, such as cognitive disorder, depression, high age, hearing and visual impairment, and the existence of other diagnoses. Special cardiovascular diseases are recognized as risk factors (Schoen et al. 2011). Other factors that canprovoke and / or broaden the risk of delirium are mechanical ventilation time, postoperative infections, operating time, pain, electrolyte disturbance, stroke or TIA, anemia, anesthesia method, and depth (Chaput & Bryson, 2012; Arenson et al., 2013). In cardiac surgery, time is deemed to be the heart-lung machine and the degree of hypotension is probable factors devoting to delirium (Smith & Dimsdale, 1989). Caring for patients with delirium can be demanding for nurses. Patients with hyperactive subtypes gravitate to be the most challenging to treat. Nurses experience different levels of stress in the management of patients with delirium. Some find it is difficult to care for patients who are not concerted, who stretch out tubes or catheters, try to get out of bed, patients who are irritated and restless or upset (McDonnell & Timmins, 2012). In a study by Yevchak et al. (2012) expressed nurses saying that the most challenging charge in the care of patients with delirium is to secure that the patient is safe. Many nurses also perceive the requirement to protect themselves.

The literature concedes that delirium is trivial after cardiac surgery. The research often concentrates on pathophysiology, predisposing causes, triggering factors, treatment methods and the patient's experiences of delirium. Theories are many about how to best care for and treat these patients. It is a patient group that can be very stringent and therefore the nurse's professionalism is denounced. Many thoughts, feelings and ethical considerations are involved in the disposal. Therefore, the main objective of our study is to determine whether the occurrences of intraoperative events in cardiac surgery are risk factors for the development of delirium in the ICU. An advance considerate of these topics can enable better recognition of patients at risk and the design of intervention studies. Endeavors to prevent delirium can have a significant effect on the health care system and patient outcomes and are an area of excessive interest in research. Delirium is a prevailing phenomenon in intensive care units. That this means increased mortality, morbidity, declined quality of life and expanded health care costs has been reported in recent years. It is thus important to determine whether recognition of early signs of delirium can be identify and thus prevent and oversee delirium through nursing appraise.

Background

Definition of delirium

Delirium is an acute organic syndrome characterized by inattention, disorientation, along with global cognitive impairment and disturbance in consciousness (Maldonado, 2008). Postoperative delirium is typically characterized by a varying rate and can be associated with either increased or decreased psychomotor activity (Maldonado, 2008). In addition, delirium-experienced patients often experience significant disorders in the sleep wake cycle (Jain, et al., 2011).

Pathophysiology of delirium

Delirium is considered to be the result of several interactive factors involving neurotransmitters, cytokines, other humoral factors as well as cerebral hypo-perfusion. Cholinergic function is an important contributor to attention, memory, excitement and fast moving sleep. These cerebral physiological functions may change if acetylcholine is insufficient. Delirium has even hypothesized that it is the result of disorders of the basic cholinergic transmission of harmful patients who have had low levels of acetylcholine (ACh) present in cerebrospinal fluid (CSF) and plasma (Flacker et al., 1998). Under normal aging, there is a decrease in the amount of acetylcholine producing cells, and as a result, less ACh (Gibson, 1981) is synthesized. Delirium may also be related to increased levels of anticholinergic activity in serum (SAA).

It has also been suggested that there may be a dose-response relationship between delirium symptoms and SAA. Delirium can also be a result of imbalance in several other neurotransmitters, which can be attributed to excess dopamine, norepinephrine and glutamate, as well as altered serotonergic and gamma aminobutyricity (van der Mast, 1996).

Some drugs have been shown to be associated with delirium. In particular, drugs with psychoactive potential, such as benzodiazepines, corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDS), opiates and chemotherapeutic agents have been shown to be a factor in delirium (Gaudreau et al. 2005). As previously mentioned, the ratio of SAA (indicating drug anticholinergic potential) (Tune et al., 1996) and the development of delirium has been demonstrated in several studies,

Incidence of delirium

The presence of delirium after cardiac surgery has been reported varies between different institutions. A review by Sockalingam et al. (2005) reported the degree of postoperative delirium to range between 2 and 72%. Variability may be due to lack of standardization of postoperative delirium identification, change of patient demographics, but also to environmental differences in each centering outcome.

Risk Factors of delirium

There are many patients and operational risk factors that have been associated with delirium. Previous studies have found that the following are particularly important. Patient-related demographic risk factors include advanced age, pre-existing dementia, hearing and impaired vision, alcohol abuse, smoking, reduced left ventricular ejection fraction, existing lung disease, hypertension, cerebrovascular disease are reported more frequently in delirium (Kazmierski, 2010, Burkhart, et al. 2010) Procedural risk factors include prolonged surgery and cardiopulmonary bypass (CPB) times, exposure to anesthesia, increased postoperative transfusion requirements, postoperative tachycardia or hypertension, atrial fibrillation, elevated blood urea and pneumonia (Bucerius, et al. 2010) .

Classification of delirium

There are three different motor subtypes of delirium: hyperactive, hypoactive and mixed. Criteria for each category were defined by Meagher et al (2000) as follows: Patients were classified as hyperactive subtype (A) if they had three or more of the following: hyper-vigilance, restlessness, fast or high speech, anger or irritability, companion unit, impatience , cohesive, swearing, singing, laughing, euphoria, wandering, light-hearted, distracting, nightmares, persistent thoughts. This subtype is the easiest recognized form but cannot be the most common. In a study by Meagher et al., Mixed was reported that the most common subtype (46%) was followed by hyperactive (30%), with hypoactive at least common (24%).

Patients were classified as the "hypoactive" subtype (B) if they had four or more of the following: unconsciousness, decreased vigilance, sparse or slow speech, drowsiness, decreased motor activity, stare, apathy. Patients were classified as "mixed" subtype if they met the criteria for both (A) and (B) above. Determining the specific subtype may be important in estimating the prognosis, as the hyper-reactive profile has been shown to be associated with shorter hospitalization and more favorable results compared to the hypoactive and mixed subtypes. This may be because hyperactive patients receive more attention and therefore better therapeutic care, or it may also be a result of the hyperactivity patients having the physical ability to be agitated (Liptzin & Levkoff, 1992).

Assessment instruments of delirium

There are different assessment tools to assess whether the patient has delirium. It is one aids in the care of patients to then decide on adequate treatment as well as early detection and treatment of delirium. Using these scales is detected even patients with hypoactive delirium. The nurse works close to the patient and is therefore well suited for carrying out the assessments (Schuurmanns, et al. 2003).

Below are some of the instruments used on ICU:

- CTD (Cognitive Test for Delirium). The instrument was designed to identify patients on ICU with delirium. Time: 10-15 minutes (Schuurmanns, et al. 2003).

- DOS (Delirium Observation Scale). Nursing's observations could screening the presence of delirium. Duration: <5 minutes (Koster, et al. 2009, Schuurmanns, et al. 2003).

- NEECHAM Confusion Scale. Developed to enable assessment of incidence of delirium without involving the patient. Based on the nurse's observation of patient during daily work. Measures 9 different factors: attention, execution of information, orientation, appearance, motor and verbal behavior, vital functions, oxygenation and urinary incontinence. Time duration: <5 min (Schuurmanns, et al. 2003, Immers, et al 2005).

- Delirium Detection Score (DDS). Developed from a scale that measures the alcoholic starch and is then developed for ICU and contains eight criteria: agitation, anxiety, hallucination, orientation, shaking, cramps, paroxysmal sweating and altered sleep and rest patterns (Schuurmanns, et al. 2003, Otter, et al. 2005).

- OBS scale (Organic Brain Syndrome scale). A psychiatric protocol. Interview with patients (Eriksson, et al. 2003).

- ICDSC (Intensive Care Delirium Screening Checklist). An instrument based on psychiatric criteria (DSM). Eight criteria where observations are made and data is collected (Bergeron, et al. 2001).

- Nu-DESC (Nursing Delirium Screening Scale). Based on five different criteria: orientation, behavior, communication, hallucinations and psychomotor activity (Gaudreau, et al 2005, Gaudreau, et al. 2005).

- CAM (Confusion Assessment Method). CAM was developed in 1990 by Inouye et al based on DSM-III-R criteria. The instrument uses a four-part algorithm (Schuurmanns, et al. 2003, Inouye, et al. 1990).

- CAM-ICU (Confusion Assessment Method for Intensive Care Unit). CAM later modified for use on intubated ICU patients using non-verbal, objective assessment tools. Duration: <5 minutes (Schuurmanns, et al. 2003).

CAM-ICU is a well-known, validated scale for assessing delirium and therefore we have chosen it for detecting delirium at ICU (Appendix 1). A modality commonly used is the value of confusion assessment method (CAM) (Inouye, et al. 1990), which in modification for use in the ICU is known as the CAM-ICU score.

CAM-lCU evaluates four separate delirium components. It defines delirium as (1) acute onset of mental status changes, (2) inattention, as well as (3) a changed level of consciousness or (4) unorganized thinking. This tool was extrapolated from the traditional CAM score to allow evaluation of mechanically ventilated patients. CAM-LCU has been found to have excellent validity, reliability, as well as interrater reliability. It is also relatively easy to perform with many publicly available exercise tools to help ICU care providers (Ely, et al., 2004).

Treatment options for delirium

Current research has shown that both non-pharmacological and pharmacological interventions can mitigate risk factors that contribute to the development of delirium (Groen et al., 2012). If possible is repeated cognitive stimulation, early mobilization as well as removal of catheters and infarts considered non-pharmacological treatment method. Also the use of hearing aids, glasses or lenses, early correction of fluid balance and good pain control are beneficial to patient (Bagri, Rico & Ruiz, 2009; Flinn et al., 2009). Access to photos, images, Calendars, watches, newspapers, TV and radio help patients to relax and improve orientation (Devlin, et al., 2011). Studies also emphasize the importance of having their relatives in near and therefore nurses should welcome and encourage close family members to be with the patient in the ICU, However, the nurse must explain to the relatives why the patient may be confused, otherwise it may be terrifying (Meagher, 2001; Yevchak, 2012).

The intensive care environment should be modified to benefit normal sleep and sleep wakefulness cycles. It is especially important to minimize noise and disturbing torques night time (Olson, 2012). According to Meagher (2001), there are more than 60% of intensive care patients who experience sleep problems. The relationship between sleep disorders and delirium has been studied for many years. Studies performed with cardiovascular patients mean that sleep difficulties are a result of delirium. McLafferty and Farley (2007) propose access to single rooms, reduced exposure to most sensory experiences, and to arrange and planning treatments can be beneficial. These measures are applied to avoid constantly disturb the patient, giving maximum periods of undisturbed sleep.

Even medical treatment is important in delirium, antipsychotic treatment, for example haloperidol, is broadly accepted and recommended by The Society of Critical Care Medicine (2002) at delirium. Haloperidol blocks the D2 dopamine receptors resulting in decrease of hallucinations, delusions, unstructured thought patterns, agitation and often also have a sedative effect (Fan et al., 2012; Girard, et al., 2008). Haloperidol is often used when the effect of the drug is rapid and has few anticholinergic drugs side effects (Brown & Boyle, 2002).

Clinics have been invited to consider alternatives medical treatments due to the adverse side effects that haloperidol may cause, examples of extrapyramidal symptoms (Atalan et al., 2013). For heart patients, however, it should have in mind that haloperidol can cause ventricular arrhythmias, prolonged QT time and cardiac arrest (Perrault, Denault & Carrier, 2000). A few years ago, dexmedetomidine was launched, one sedative drug to be used postoperatively after surgery. Jakob et al. (2012) describes two randomized studies comparing efficacy between dexmedetomidine and midazolam / propofol in patients with prolonged respiratory time. The results showed that Dexmedetomidine reduced delirium, agitation and anxiety. Sanders & Maze, (2011) mean that dexmedetomidine causes less memory and allows for more natural sleep. Propofol is also a drug commonly used in intensive care. Segatore, et al., (1998) believe that Propofol may be a useful preparation when postoperative delirium is so serious that the patient's life is threatened. Propofol can help to quickly get control of the situation but do not solve the basic problem.

Chapter Two
Literature Review

Literature review

ICU Delirium Risk Factors

Risk factors for delirium could be prorated into predisposing factors and precipitation factors (Girard et al. 2008; Pun and Ely 2007; Inoye and Charpentier 1996). Predisposing factors prevail before intensive care unit entrance and are difficult to transform, while precipitation factors occur all along critical sickness and may be fluctuating. Miller and Ely (2006) suggested three classes of risk factors for delirium progress: a) predilection or baseline susceptibility; (b) foundation risk factors such as the countenance of the acute illness; and (c) hospital- analogous or factors that is caused by a medication or health care providers.

Afonso et al. (2010) constitute an anticipating design for delirium postoperatively in one hundred and twelve heart surgery patients. Surgery comprised CABG, valve replacement and aortic operations. The percentage of delirium was thirty four percent. Increased age and increased duration of operation were the greater influential risk factors for delirium after surgical operation. Detroyer et al. (2008) studied delirium postoperatively in one hundred and four patients concentrating on anxiety and depression at the time that risk factors for delirium after surgery.

Bakker et al. (2014) investigated delirium forecasters after heart surgery in two hundreds and one patients. A mini-mental status examination (MMSE) was applied to assess the cognitive function of the patients before operation and medical charts were appraised (Bakker, et al. 2014).

As a conclusion, logistic regression model, lower MMSE scores, greater creatinine altitudes, and lengthy extracorporeal circulation time were outlying prognosticator of delirium. Mortality rates in the first thirty days after surgery were significantly higher in delirium patients (14% versus 0%) compared to non-delirium patients.

In a retrospective trial by Andrejaitiene and Sirvinska's (2012) determining risk factors for delirium after heart surgery. Participants were studied as two recognizable groups: mild to moderate delirium and severe delirium. It was shown that utilization of a dose of fentanyl over 1.4 mg elevated the probability of progressing severe delirium. Lengthy aortic clamping time was also observed as a predominate prognosticator of severe delirium. Atrial fibrillation likewise appeared oftentimes in participants with severe delirium than those with mild to moderate delirium.

The trial by Schoen et al. (2011) intended to explore preoperative and intraoperative cerebral oxygen saturation and its incorporation with delirium postoperatively in participants go through heart surgery. Two hundreds thirty one participants were enrolled into the study. Cerebral oxygen saturation was evaluated applying cerebral oximetry, recognizing “disparity in cerebral oxygen supply / demand". Elder, lower MMSE scores, neuropsychiatric disorder, and reducing cerebral oxygen saturation preoperatively were independent forecaster of delirium after operation.

Pandharipande et al. (2006) studied sedatives and analgesics as risk factors for participant's transformation to delirium. One hundred and ninety-eight mechanically ventilated participants were enrolled to coronary critical care units. Using a Markov regression model, lorazepam was found to be an independent risk factor for daily delirium transition, alternative sedatives and analgesics, such as midazolam, fentanyl, morphine and propofol, were not significant, even though the evidence they were combined with trends towards significance.

The association between nurse-administered midazolam and event of delirium was determined by Taipale et al. (2011) in a descriptive trial. One hundred and twenty-two participants who underwent heart surgery were enrolled to the trial. In this ICU context, there were no rigorous sedation guidelines other than the physician's existing orders and sedatives were given when patients needed it. The authors were shown that for each milligram of midazolam added, participants were 7-8% more ancestors of progress delirium.

Chang, et al (2019) performed a trial to compare the divergence of characteristics in participants with and without delirium and to characterize risk factors combined with delirium in patients introduced to an intensive care unit after heart surgery. A retrospective chart review was utilized to gather data on two hundreds eighty patients who operated for open heart surgery. A set up inventory of fifty two patient-related risk factors for delirium was utilized to assemble pre- intra- and postoperative data.

All patients were assessed by psychiatrist and delirium was diagnosed confer to the criteria in the Diagnostic and Statistical Manual of Mental Disorders, fourth edition. The occurrence of delirium postoperatively was 41.7%. Participants with and without delirium diverge significantly in twenty nine variables. Four factors postoperatively were come up; hematocrit less than thirty percent, cardiogenic shock, hypo-albuminemia and acute infection, were significant, independent prognosticator of delirium postoperatively. The authors were concluded that the endorsement of such a checklist can expedite the capability to prevent or encounter delirium early and enforce disbursed treatment.

Kumar, et al (2017) organized a study, which purposed to determine the occurrence, motor subtypes, and risk factors combined with delirium progress in heart surgery participants who were enrolled to postoperative cardiac critical care using a substantiated delirium overseeing tool. The trial involved one hundred twenty patients who had been pretended to go through heart surgery. Explicit pre- intra- and postoperative data for conceivable risk factors were collected. One time a day, an evaluation of delirium was elaborated. Delirium was noticed in 17.5% of patients. Greater of cases were of the hypoactive delirium type (85.72%).

Considerable risk factors were found to be combined with delirium and five independent variables were disclosed. History of high blood pressure, carotid artery disorders in the form of stroke or bleeding, non-invasive ventilation, resting for more than 10 days in the ICU and poor pain control postoperatively were combined with delirium in the post-heart surgery patients.

Richford et al (2012) implemented a study to assess the literature on drugs combined with delirium after heart surgery and probable prophylactic agents to deter it. Articles explored in different data bases. Fifteen studies were revised. Two drugs (intraoperative fentanyl and ketamine) and two drug categories (preoperative antipsychotics and postoperative inotropes) were tenacious in the literature as independently combined with delirium after heart surgery. Accession seven classes of drugs (preoperative antihypertensive, anticholinergic, antidepressant, benzodiazepines, opioids and statins and postoperative opioids) and three drugs (intraoperative diazepam and postoperative dexmedetomidine and rivastigmine) have blended outcomes. A drug (risperidone) has been found to prevent delirium when taken directly after arousal from the heart surgery. These studies have shown that drugs allotted by patients with heart surgery must be taken in concern in risk management strategies for delirium.

Rudinger, et al., (2016) implemented a retrospective cohort study to determine if intraoperative pathophysiological fluctuation and therapeutic interference influence the risk of delirium postoperatively. The diagnosis of delirium was evaluated with approved scores.

Comparisons between patients with and without delirium were accomplished. Of the one hundred ninety four consecutive patients after heart surgery, 50 (26%) progressed delirium all along their ICU stay. Univariate analysis disclosed that significant variations between participants with and without delirium appeared in the ensuing intraoperative variables: period of cardiovascular bypass, lowest mean arterial pressure, lowest hemoglobin level), lowest body temperature, highest noradrenaline support and total of red blood cell and platelet transfusions. Alone platelet transfusions continued an independent risk factor in the multivariate assay. The authors concluded that in patients undergoing heart surgery, various intraoperative assets, such as platelet transfusion, were risk factors for the progression of a delirium postoperatively in the ICU. Expedite research is required to disclose the underlying mechanisms.

McPherson, et al., (2013) implemented a study to examine the prevalence and risk factors for delirium amongst CVICU participants. It was a descriptive trial. Two hundred subsequent patients with a planned CVICU stay more than 24 hours were registered. Demographic details and daily assessment for delirium applying the validated and reliable method of evaluation of intensive care confusion (CAM-ICU) was documented and calculable follow-up of delirium risk factors was implemented. Separate analyzes tested the aspect of entry risk factors for the instance of delirium during CVICU. The percentage of delirium was 26%. Approximately all ninety two percent conferred the hypoactive delirium subtype.

Benzodiazepine usage was anticipated for a 3-fold heightened risk of delirium during the CVICU stay. Of the daily risk factors, it was similar that patients receiving benzodiazepines or having restrictions or devices that prevented mobilization had delirium the following day. Hemodynamic status was not combined with delirium. The authors concluded that delirium appeared in one of four patients in CVICU and was broadly hypoactive in subtype.

From the literature review above, we have noticed that there are alterations in the occurrence of delirium postoperatively, predisposing and precipitating factors for delirium in different studies and different assessment instruments of delirium. It seems that different institutions had different incidence and different predisposing and precipitating factors for delirium. In addition, delirium does not have a sole cause, but is better characterized as having a multifactorial and divergent mechanisms.

Chapter Three
Methodology

Research Methodology

Design: A descriptive analytical design.

Setting: The study was conducted at cardiac surgery ICU at A Najah National University Hospital, Ramallah State Hospital and Al-Ahli Hospital in the West Bank.

Population and selection

We conducted a prospective study. The population of this study includes 60 male and female patients consecutively admitted after cardiac surgery to cardiac intensive care units over a 6-month period from May 1, 2018 to November 30, 2018, approved by the Institutional Review Board (IRB) for the study from An-Najah National University and the requirement of patient consent was revoked. Information collected included patients' demographics, preoperative comorbidities and intraoperative variables, and postoperative complications. These variables and complications were analyzed to determine their association with delirium. The diagnosis of delirium is clinically established using the Confusion Assessment (CAM-ICU) and the Richmond Agitation and Sedation Scale (RASS).

The researcher created a link with the hospital managers to request the participation of patients in the study conducted at three hospitals on the West Bank (located north, middle and south of the West Bank). The information sheet was filled in at the selected patients after agreeing to participate in the study.

Inclusion criteria

The participants are patients (male and female) between the ages of 18 and 70, who undergo elective surgery for coronary artery disease, valvular placement / repair and other open heart surgeries at the three hospitals.

Exclusion criteria

- patients with pre-operative delirium screening during preoperative evaluation of the Confusion Assessment Method (CAM);
- those with mechanical ventilation,
- those who refuse consent.
- patients who did not have heart surgery in hospital.

Data Collection

A detailed clinical data sheet form is created to gather relevant data to determine the effect of preoperative, intraoperative, and postoperative variables on delirium. Baseline demographics and information on pre-release risk factors for delirium were obtained at inclusion. Potential risk factors were identified from a review of the literature of surgical ICU patients and post-cardiac surgical patients, as well as from meetings with CVICU staff. A researcher designed a data sheet with patient-related risk factors for delirium was used to collect preoperative, intraoperative and postoperative data. The data sheet was based on the results of previous studies (Lou, et al., 2004; Bucerius, et al., 2004; Böhner, et al., 2003; Marcantonio, et al., 1998; Van der Mast et al. , 1996; Winawer et al., 2001; Koivula, et al., 2001).

A review of the data sheet was conducted by a panel of three cardiac intensive care nurses, two anesthesiologists and a statistician to select the best for the clarity of the data sheet, the accuracy of the measured knowledge and interpretability provided a content validity. After some modifications, the data sheet was ready for use

Baseline demographic and information on risk factors for delirium were obtained age, gender, education, smoking and marital status.

Preoperative data

Specific preoperative data such as history of abuse, stroke, renal impairment. Medical disorders are obtained such as valvular heart disease, coronary heart disease, hypertension, diabetes, kidney failure, thyroid disease, depression, left ventricular ejection fraction (LVEF) less than 30, atrial fibrillation, hearing and visual impairment, cardiogenic shock‹New York Heart New York Heart Association (NYHA) Classification 3 or 4, pulmonary arterial hypertension, depression, arterial disease, preoperative statin use, psychoactive potential medications such as benzodiazepines, corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDS), opiates and chemotherapeutic agents, anticholinergic potential and opiates (Appendix 2).

Intraoperative data

Temperature is measured, Blood transfusion, fresh frozen plasma and platelet transfusion, amount of inducing agent (propofol, midazolam, ketamine), use of phenylephrine, use of morphine and fentanyl, cardiopulmonary bypass time (CPB), aortic cross-clamp time, and use of inotrope are obtained, extubation in the operating room or postoperative is noted.

Postoperative data

Re-surgery, total mechanical ventilation time, atrial fibrillation, fresh frozen plasma, platelets and blood transfusion, cardiogenic shock, post-operative infection, bilirubin> 2 mg / dl, creatinine> 3 mg / dl, Hb, use of atropine, Na> 140, mEq , PaO2 <70 mmHg, prolonged hypotension, measurement of temperature, postoperative tachycardia, intra-aortic balloon pump use (IABP) and insomnia, hematocrit <30, total amount of midazolam, bolus doses of morphine, postoperative pain rated using VAS , postoperative chest drainage volume, non-invasive ventilation use, days spent in ICU, ,sequential organ failure assessment score (SOFA)), use of inotropic postoperatively are noted

Delirium Assessment

Delirium (main outcome variables):

Patients with delirium are identified by the CAM-ICU (Appendix 1). The pooled sensitivities and specificities for detecting delirium in critically ill patients are 76% and 96%, respectively, for CAM-ICU [Ely, et al., 2001, Neto, et al., 2012). In the current study, a positive screening initiated a diagnostic work that led to confirmation (or refusal) of the delirium diagnosis.

The motor subtype was classified as hypoactive, hyperactive or mixed according to the patient's behavior

Patients in consecutive delirium evaluations were routinely performed on a 24 hour basis using the Confusion Assessment (CAM-ICU). The assessment was carried out for up to three days in the ICU. Delirium assessment is performed by the ICU nursehave been informed about the points and how they should be used before the study was conducted.

The RASS scale (Appendix 3) is used in the CAM-ICU to define motor subtypes of delirium. Patients with CAM-ICU positive and RASS score positive (+1 to +4 for each evaluation are considered to have hyperactive delirium; in these patients, delirium in the form of hyperactive "subtype (A) was manifested if they had three or more of the following: restlessness, fast or loud talk, anger or irritability, fighting power, impatience, un-cooperability, swearing, singing, laughing, euphoria, walking, slightly astonishing, distractibility, nightmares, persistent thoughts. Those with CAM-ICU positive and RASS-negative (0- -3) at each evaluation is considered to have hypoactive subtype (B) delirium, this was manifested as having four or more of the following: ignorance, diminished alertness, scanty or slow speech, lethargy, decreased motor activity, staring, apathy. Patients who, during their ICU course, were found to be delirious on at least one occasion who exhibited positive symptoms (hyperactive or "high" delirium) while on at least one other occasion who exhibited negative symptoms (hypoactive, "silent" or invisible delirium)

was considered to have mixed delirium. All patients who tested positive are then referred to as cases and the other subjects are considered to be in control. The delirium diagnosis is documented in the patient's medical notes.

Data are presented as mean ± standard deviation. Binary outcome variables were defined for each positive delirium event that occurred during the patient's stay in the ICU. Patients with delirium were compared with those without delirium in terms of their demographic and other perioperative parameters.

Anesthesia protocol

Anesthesia management was performed according to the standard institutional protocol. The selection of monitors, choice of induction agents for anesthesia and maintenance of anesthesia was submitted to the participating team. Data were obtained on each of these facets according to the attached data sheet. The anesthetist had tried to keep the mean arterial pressure within ± 20% of the baseline or an average arterial pressure> 60 mmHg; the choice of vasopressors, inotropes, and vasodilators was provided to the current anesthetic gene. pH management was used. Surgery was performed under mild hypothermia to normothermia (32 ° C - 36 ° C).

The patients were moved to the ICU following the procedure for mechanical ventilation. Titrated doses of propofol / midazolam and bolus doses of morphine were used during the postoperative period. Patients were weaned from mechanical ventilation at the discretion of ICU physicians

Procedure

Institutional Review Board approval for the obtained study and the requirement for patient consent was revoked. Information collected included patient demographics, preoperative comorbidities and intraoperative variables, and postoperative complications (see Appendix 1 for full clinical report form). These variables and complications are analyzed to determine their association with delirium. Sixty patients who underwent elective surgery for coronary artery disease and valve replacement / repair are included in this study. Exclusion criteria include patients with pre-existing delirium at screening in preoperative evaluation of the method of confusion assessment (CAM) and those who refuse consent. Specific preoperative data, such as history of abuse, stroke, kidney function and other medical disorders are obtained. Anesthesia management is done according to the standard institutional protocol. The choice of monitors, the choice of anesthetic induction agents and the maintenance of anesthesia are left to the participating team. Data were obtained on each of these facets according to the attached data sheet. The anesthetist has attempted to keep the average arterial pressure within ± 20% of baseline or mean arterial pressure> 60 mmHg; the choice of vasopressors, inotropes and vasodilators was left to the anesthetic strain. Surgery is performed

under mild hypothermia to normothermia (32 ° C - 36 ° C). Patients are transferred to the ICU following the mechanical ventilation procedure. Iterated doses of propofol / midazolam and bolus doses of morphine were used during the postoperative period. Patients are weaned from mechanical ventilation in the creation of the ICU physician. The patients sequentially recorded evaluations of delirium performed on 24 hours using the confusion assessment method (while in ICU) and RASS. The assessment is performed in the ICU to determine the presence or absence of delirium. Daily laboratory data and information on exposure to medication and anesthesia were collected during the patient's CVICU stay.

Data analysis

The statistical software used is the Statistical Package for Social Sciences (SPSS) 21. Continuous variables were analyzed using descriptive statistics (mean, standard deviation); categorical data were analyzed as proportions (number, percent). The test used to prove the relation between delirium and pre-operative factors was Chi – square. To test the association between the delirium and demographic, pre, intra, and post-operative factors, the chi- square was used to test if categorical demographic variables are predictor of delirium cases, and 2 independent samples t-test was used for scale demographic variables.

Ethical consideration

The study follows the World Health Organization Declaration of Helsinki on the Ethical Principles of Helsinki for Medical Research on People (World Medical A. (2013). The study was approved by the Palestinian Ministry of Health, hospital administration and An-Najah National University's IRB. Dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research participants were considered. The participants were adequately informed about the goals, methods, possible conflicts of interest, the institutions' connection to the researcher, the expected benefits and potential risks of the study and any discomfort it may entail.

Participants were informed about the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisals. Particular attention was paid to the participants' specific information needs as well as the methods used to deliver the information. After ensuring that the participants understood the information, the researcher sought the participant's freely given informed consent, in writing.Data were collected using the study data sheet. Participants were informed that data collected will only be used for research purposes

Chapter Four
Results

Sixty patients who underwent elective cardiac surgery and were subsequently admitted to cardiac surgical ICU were enrolled into this study. All subjects were screened for delirium using the CAM‑ICU test once daily, and all those who tested positive were thereafter designated as cases and the other subjects were deemed controls. Among 60 patients, 75.9% (41/54) patients were found to have delirium and 24% (13/54) patients were delirium free in the same day of surgery. 35.2% (19/54) had delirium in the first day of surgery. Hyperactive type of delirium was seen in 22/41 patients (54.7%) while 11/41 patients (25.9%) had hypoactive delirium and 6/41 (13%) patients had mixed delirium.

A purposeful sample of 60 patients who underwent an on-pump open heart surgery was included in the study, three hospitals were targeted in this study in the West Bank (located at north, middle and south of the West Bank). For exclusion, patients with delirium were identified by using the CAM-ICU assessment tools, those who were identified with delirium were excluded from the study as the surgery might not be the main cause of the delirium otherwise the patient is included, all of the 54 patients were identified with no delirium, 6 patients were excluded for not completing the required data

Sample descriptive Statistics

Table (1) below describes the sample properties in terms of education, smoking status, gender, marital status and age, the table shows that 66.7% of the patients were not holding university degrees, half of the patients were smokers, 68.5% were male patients, only 5.7% of the patients were unmarried and the mean age of the patients was 57.7 years

Table 1: Sample properties presented by counts and percentage

Variable	Categories	Counts	%
Education	Tawjihi or less	36	66.7%
	University	18	33.3%
Smoking status	Yes	27	50.0%
Gender	Male	37	68.5%
	Female	17	31.5%
Marital status	Unmarried	3	5.7%
	Married	50	94.3%
Age (mean)	57.72±1.329		

Figure (1) shows some of pre-operative descriptive statistics for a set of diseases for the participants (indicators), the orange bars in the figure represent those who have the disease.

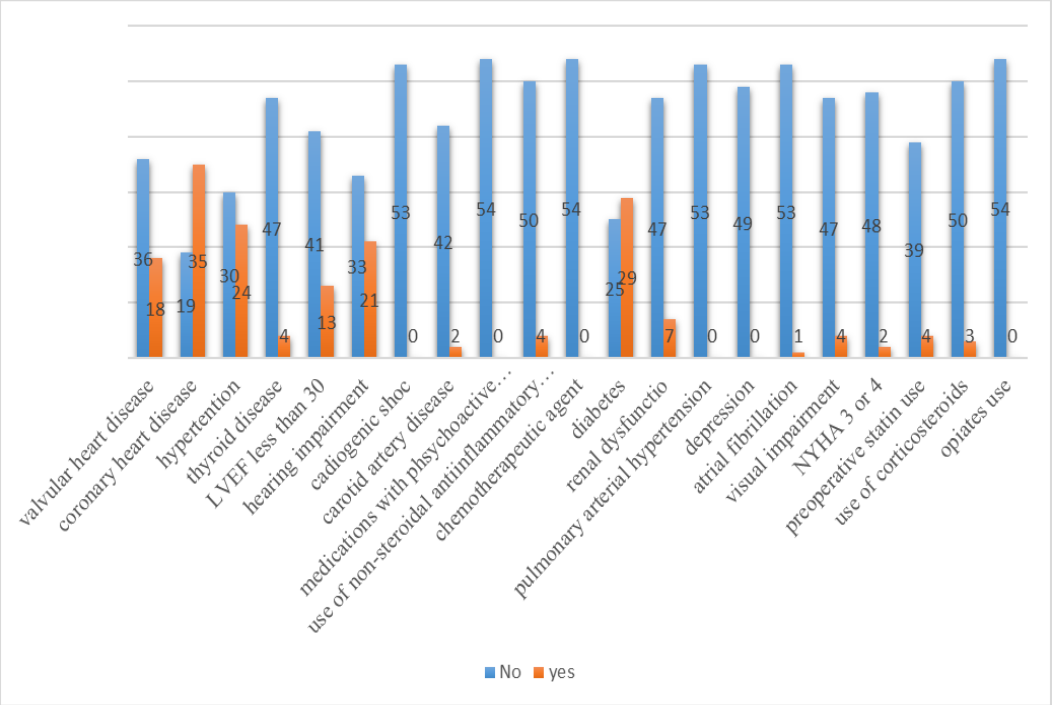

Figure 1: Descriptive statistics for pre-operative indicators (frequencies)

Figure 1 shows that about 65% (35 patients) of the sample have coronary disease, about 54% (29 patients) of the sample have diabetes, about 44% (24 patients) have hypertension, about 39% (21 patients) have hearing impairment, about 33% (18 patients) of them have valvar heart disease, while no one of the sample have depression, pulmonary arterial hypertension, opiates use, chemotherapeutic agent, cardiogenic shock, medications with psychoactive potential.

Intra operative interventions

Figure (2) shows intra operative interventions.

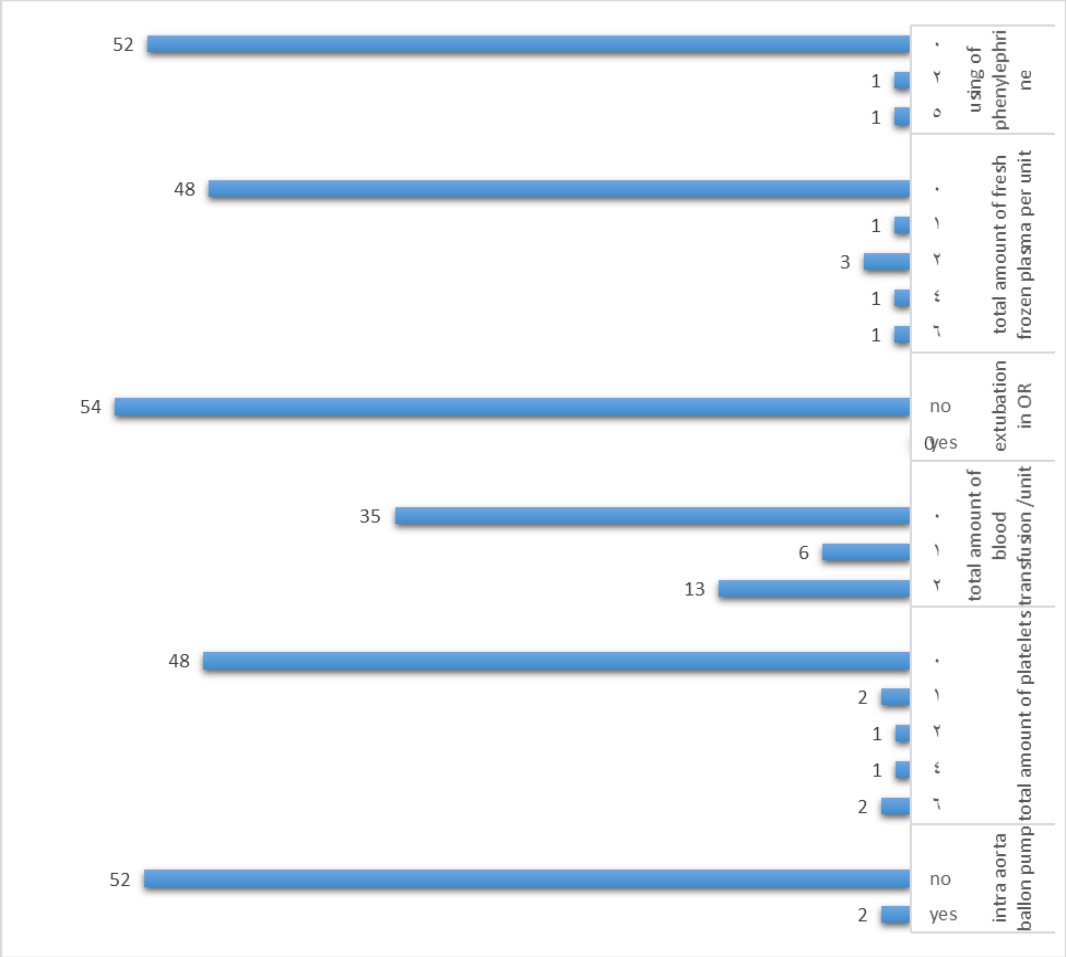

Figure 2: Intra operative interventions

Figure two shows that there was one patient who received twice phenylephrine and another patient who received five times. Regarding the number of frozen plasma units, there are three patients who received 2 units, one patient received four units and one patient received six units. Six patients received blood transfusion of one unit and 13 patients of two units. Two patients were required intra-aortic balloon pump (Figure 2).

Table 2: Shows the mean, Standard error of mean and standard deviation for the scale interventions that has been done intraoperative.

Indicator	Mean	Std. Error of mean	Std. Deviation
Total amount of midazolam/mg	2.63	.148	1.087
Total amount fentanyl/µg	383.04	23.617	171.935
Cardiopulmonary bypass (CPB) time/min	111.09	3.151	23.153
Total amount of ketamine /mg	39.40	2.910	21.184
Total amount of morphine/mg	7.43	.434	3.190
Total amount of propofol/mg	95.32	4.644	33.808
Aortic cross-clamp time/min	96.50	4.151	30.506

In table (2), mean (SD) of Total amount of midazolam/mg 2.63 (1.087), Total amount fentanyl/µg 383.04 (171.935), Cardiopulmonary bypass (CPB) time/min 111.09 (23.153), Total amount of ketamine /mg 39.40 (21.184), total amount of morphine/mg 7.43 (3.190), Total amount of propofol/mg 95.32 (33.808), Aortic cross-clamp time/min 96.50 (30.506).

Post –Operative Delirium

After the operation, each of the patients had to answer the Confusion Assessment Method for the ICU (CAM-ICU), to help decide whether the patient has developed delirium or not, table (3) below shows the percentages of patients who developed delirium after the operation and the three days following the operation.

Table 3: Incidence of post-operative delirium. Data is presented as counts and percentage

Status	Post-operative day (0)	Post-operative day (1)	Post-operative day (2)	Post-operative day (3)
Delirium%	75.9%	35.2%	3.7%	3.7%
Counts	41	19	2	2

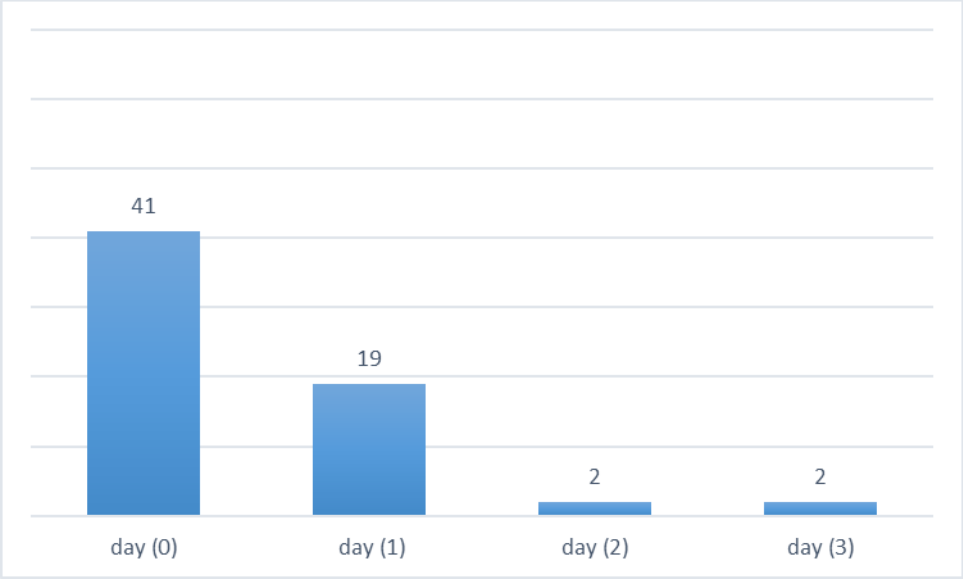

Figure 3: incidence of post-delirium (counts)

As of the above table and Figure3, those who developed delirium right after the operation were 75.9% (41 patients) of the targeted sample, the percentage continued to drop until it reached 3.7% (2 patients) in the second and third day.

To have a closer look to when the delirium was developed table (4) shows the day when delirium started and when the symptoms disappeared, the table (4) shows that almost half of the patients (46.3%) (25 patients) developed delirium after the operation and by the first day after the operation the symptoms disappeared, while about a quarter of the patients developed it right after the operation 25.9% (14 patients) and two days after the surgery the symptoms disappeared

Table 4: Delirium Development Day

Day(0)	Day(1)	Day(2)	Day(3)	Counts	Percentage
No Delirium	No Delirium	No Delirium	No Delirium	7	13.0%
Delirium	No Delirium	No Delirium	No Delirium	25	46.3%
No Delirium	Delirium	No Delirium	No Delirium	4	7.4%
Delirium	Delirium	No Delirium	No Delirium	14	25.9%
Delirium	No Delirium	Delirium	No Delirium	1	1.9%
No Delirium	Delirium	Delirium	No Delirium	1	1.9%
No Delirium	No Delirium	No Delirium	Delirium	1	1.9%
Delirium	No Delirium	No Delirium	Delirium	1	1.9%

Delirium association with demographic variables, pre, intra, and post-operative interventions

To test the association between the delirium and demographic, pre, intra, and post-operative factors, the chi- square was used to test if categorical demographic variables are predictor of delirium cases, and 2 independent samples t-test was used for scale demographic variables. Tables (5-8) below show the control (patients with no delirium detected) and the cases (patients with delirium detected)

Depending on the tables below and at 95% confidence level our data shows that:

- No relation could be detected between delirium and the demographic variables (education, smoking status, gender, marital status and age)(table 5)
- No relation could be detected between delirium and the pre-operative factors given that highlighted variables such as cardiogenic shock. Depression and chemotherapeutic agent could not be tested because none of the patients experienced such a condition.(table 6)
- Amongst the intra operative factors total amount of midazolam and morphine usage were of a significant relation with developing delirium. (table 7)
- Amongst post-operative interventions use of atropine, temperature, Bolus doses of morphine and SOFA were of significant relations with developing delirium. (Table 8)

Demographic variables

The patients were classified as “cases group”, those who were classified as cases suffered from delirium, and the others belonged to the control group, the day after the operation 13 patients were in control group, and 41 were in cases group.

Table 5: categorical demographic factors. The chi- square was used to test if categorical demographic variables are predictor of delirium cases, and 2 independent samples t-test was used for scale demographic variables.

Variable	Categories	Number of patients				P
		N=13		N=41		
		Control (non-delirium)		Cases (delirium)		
		counts	%	Counts	%	
Education	Secondary or less	8	61.5%	28	68.3%	0.653
	University	5	38.5%	13	31.7%	
Smoking status	No	5	38.5%	22	53.7%	0.340
	Yes	8	61.5%	19	46.3%	
Gender	Male	10	76.9%	27	65.9%	0.685
	Female	3	23.1%	14	34.1%	
Marital status	Unmarried	0	0.0%	3	7.5%	0.745
	Married	13	100.0%	37	92.5%	
Age		57.85±2.28		57.68±1.61		0.959

- Corrected chi square

Pre-operative factors

As mentioned previously the test used to prove the relation between delirium and pre-operative factors was Chi – square. In table (6) below indicates the significance of the relation in the case of cardiogenic shock, medications with psychoactive potential such as benzodiazepines, chemotherapeutic agent, pulmonary arterial hypertension, depression, and

opiates use. The relation could not be tested as all the sample patients have not experience any of these conditions. For the rest of the variables P-values were all greater than 0.05 which indicates that the relation between delirium and pre-operative factors could not be proven significant under the confidence interval level of 95%.

Table 6: pre-operative factors

		Number of patients				P
		N=13		N=41		
		Control (non-delirium)		Cases (delirium)		
		Counts	%	Counts	%	
Valvar heart disease	No	7	53.8%	29	70.7%	0.260
	Yes	6	46.2%	12	29.3%	
Coronary heart disease	No	2	15.4%	17	41.5%	0.167
	Yes	11	84.6%	24	58.5%	
Hypertension	No	6	46.2%	24	58.5%	0.434
	Yes	7	53.8%	17	41.5%	
Thyroid disease	No	12	100.0%	35	89.7%	0.588
	Yes	0	0.0%	4	10.3%	
LVEF less than 30	No	9	69.2%	32	78.0%	0.783
	Yes	4	30.8%	9	22.0%	
Hearing impairment	No	8	61.5%	25	61.0%	0.971
	Yes	5	38.5%	16	39.0%	
Cardiogenic shock	No	13	100.0%	40	100.0%	
	Yes	0	0.0%	0	0.0%	
Carotid artery disease	No	8	100.0%	34	94.4%	1.00
	Yes	0	0.0%	2	5.6%	
Medications with psychoactive potential such as benzodiazepines	No	13	100.0%	41	100.0%	
	Yes	0	0.0%	0	0.0%	
Use of non-steroidal anti-inflammatory agents (NSAIDS)	No	13	100.0%	37	90.2%	0.574
	Yes	0	0.0%	4	9.8%	
Chemotherapeutic agent	No	13	100.0%	41	100.0%	
	Yes	0	0.0%	0	0.0%	
Diabetes	No	4	30.8%	21	51.2%	0.332
	Yes	9	69.2%	20	48.8%	
Renal dysfunction	No	12	92.3%	35	85.4%	0.861
	Yes	1	7.7%	6	14.6%	
Pulmonary	No	12	100.0%	41	100.0%	

		Number of patients				P
		N=13		N=41		
		Control (non-delirium)		Cases (delirium)		
		Counts	%	Counts	%	
arterial hypertension	Yes	0	0.0%	0	0.0%	
Depression	No	12	100.0%	37	100.0%	
	Yes	0	0.0%	0	0.0%	
Atrial fibrillation	No	12	92.3%	41	100.0%	0.540
	Yes	1	7.7%	0	0.0%	
Visual impairment	No	13	100.0%	34	89.5%	0.535
	Yes	0	0.0%	4	10.5%	
NYHA 3 or 4	No	13	100.0%	35	94.6%	0.974
	Yes	0	0.0%	2	5.4%	
Preoperative statin use	No	7	77.8%	32	94.1%	0.392
	Yes	2	22.2%	2	5.9%	
Use of corticosteroids	No	13	100.0%	37	92.5%	0.745
	Yes	0	0.0%	3	7.5%	
Opiates use	No	13	100.0%	41	100.0%	
	Yes	0	0.0%	0	0.0%	

Intra operative factors

Chi square test was used to test the significance of the relation between delirium and intraoperative factors in the case of categorical intraoperative variables in table (7), while t-test is used to test the scale variables as could be seen in table (8), none of the sample patients was extubated in OR so the relation with delirium could not be tested as a result, when having a look at the p-values we can see that only two variables were proven significant in relation to delirium which are total amount of midazolam/mg in control group 3.31±0.398 compared to 2.41±.135 in delirium group, p= .051, (95% confidence level) and the result shows that those who did not suffer from delirium have had higher amount of midazolam/mg and this was proven significant (Table 7).

This result indicates that Midazolam is a protective drug against delirium. There was a significant difference at (90% confidence level) in the total amount of morphine/mg in control group (no delirium) 8.85±1.04 compared to delirium group 7.93±.45 (p= .085), those who took more morphine/mg where more likely not to develop delirium after the surgery (Table 8). This result indicates that Morphine is a protective drug against delirium.

Table 7: Intra-operative factors (categorical variables)

P- value Variable		Number of patients				P- value
		N=13		N=41		
		Control (non-delirium)		Cases (delirium)		
		Counts	%	Counts	%	
Using of phenylephrine	0	12	92.3%	35	97.2%	.207
	2	0	0.0%	1	2.8%	
	5	1	7.7%	0	0.0%	
Total amount of fresh frozen plasma/unit	0	12	92.3%	33	86.8%	.323
	1	0	0.0%	1	2.6%	
	2	0	0.0%	3	7.9%	
	4	0	0.0%	1	2.6%	
	6	1	7.7%	0	0.0%	
Extubating in OR	No	13	100.0%	41	100.0%	
	Yes	0	0.0%	0	0.0%	
Total amount of blood transfusion/unit	0	9	69.2%	26	63.4%	.647
	1	2	15.4%	4	9.8%	
	2	2	15.4%	11	26.8%	
Total amount of platelets	0	12	92.3%	36	87.8%	.731
	1	0	0.0%	2	4.9%	
	2	0	0.0%	1	2.4%	
	4	0	0.0%	1	2.4%	
	6	1	7.7%	1	2.4%	
Intra aorta balloon pump	No	13	100.0%	39	95.1%	1.00
	Yes	0	0.0%	2	4.9%	

Table 8: intra-operative factors (scale variables)

Variable	Number of patients		P- value
	N=13	N=41	
	Control (non-delirium)	Cases (delirium)	
Total amount of midazolam/mg	3.31±0.398	2.41±.135	.051
Total amount fentanyl/mg	397.31±51.778	378.40±26.740	.734
Cardiopulmonary bypass (CPB) time/min	111.92±7.549	110.83±3.449	.884
Temperature	33.38±.65	32.36±0.30	.117
Total amount of ketamine /mg	36.92±5.93	7.93±.446	.633
Total amount of morphine/mg	8.85±1.04	7.93±.45	.085
Total amount of propofol/mg	90.77±7.77	96.80±5.32	.581
Aortic cross-clamp time/min	91.69±4.88	98.02±5.25	.519

Post-operative

In table 9, Same procedure was undergone through to test the relation between post-operatives variables and delirium, and the variables with significant relation to delirium were use of **atropine** (90% confidence level) as those who seemed to use more atropine were significantly less likely to develop delirium, as in control group (not delirium) 3 (23.1%) patients received atropine compared to delirium group 1 (2.4%), p= 0.062. This result indicates that Atropine is a protective drug against delirium.

Regarding temperature **(**95% confidence level) those patients who had low grade or high temperature 19(46.3) in delirium group compared to 0(0%) in the control group (p= 0.01) were significantly more likely to develop delirium (Table 9). This result indicates that low grade or high temperature is a precipitating factor for delirium. Bolus doses of

morphine/mg (95% confidence level) as in the control (not delirium) M(SD) .00±.000 compared to 1.17±.308 in the delirium group, p= (0.001) those patients who took morphine where significantly more likely to develop delirium. Regarding the sequential organ failure assessment score (SOFA) (90% confidence level) as those patients who scored higher SOFA in the delirium group 5.56±.191were more likely to develop delirium compared with control group (not delirium) 4.85±.390, (p= 0.083) as shown in table (10). This result indicates that higher SOFA was a precipitating factor for delirium.

Table (9): post- operative factors (categorical variables)

Variable	Categories	Number of patients				P
		N=13		N=41		
		Control (non-delirium)		Cases (delirium)		
		Counts	%	Counts	%	
Reoperation	No	13	100.0%	37	92.5%	0.745
	Yes	0	0.0%	3	7.5%	
The total time on mechanical ventilation/hr	0	1	0.00%	0	0.00%	0.174
	<12h	11	92.3%	40	97.6%	
	(12-24) h	1	7.7%	0	0.0%	
	(25-48) h	0	0.0%	0	0.0%	
	(49-72) h	0	0.0%	0	0.0%	
	<3days	0	0.0%	1	2.4%	
Atrial fibrillation	No	12	92.3%	40	97.6%	0.975
	Yes	1	7.7%	1	2.4%	
Blood transfusion	No	9	69.2%	21	51.2%	0.413
	Yes	4	30.8%	20	48.8%	
Platelet transfusion	No	12	92.3%	36	87.8%	1.00
	Yes	1	7.7%	5	12.2%	
Cardiogenic shock	No	13	100.0%	40	97.6%	1.00
	Yes	0	0.0%	1	2.4%	
Postoperative infection	No	13	100.0%	39	97.5%	1.00
	Yes	0	0.0%	1	2.5%	
Na> 140, neq	No	9	69.2%	30	73.2%	1.00
	Yes	4	30.8%	11	26.8%	
Prolonged hypotension	No	12	92.3%	36	87.8%	1.00
	Yes	1	7.7%	5	12.2%	

Variable	Categories	Number of patients				P
		N=13		N=41		
		Control (non-delirium)		Cases (delirium)		
		Counts	%	Counts	%	
Sleep deprivation	No	9	69.2%	17	43.6%	.2
	Yes	4	30.8%	22	56.4%	
Fresh frozen plazma-day1	No	12	100.0%	35	85.4%	0.374
	Yes	0	0.0%	6	14.6%	
Intra-aortic balloon pumb-day1	No	13	100.0%	38	95.0%	1.00
	Yes	0	0.0%	2	5.0%	
Bilirubin > 2 mg /dl	No	13	100.0%	39	95.1%	1.00
	Yes	0	0.0%	2	4.9%	
Use of atropine	No	10	76.9%	40	97.6%	0.062
	Yes	3	23.1%	1	2.4%	
Postoperative tachycardia	No	6	46.2%	23	56.1%	0.531
	Yes	7	53.8%	18	43.9%	
Hematocrit<30	No	7	53.8%	15	36.6%	0.270
	Yes	6	46.2%	26	63.4%	
Postoperative pain VAS >=4	No	7	53.8%	17	41.5%	0.434
	Yes	6	46.2%	24	58.5%	
Creatinine>3mg/dl	No	11	84.6%	37	90.2%	0.955
	Yes	2	15.4%	4	9.8%	
Temperature	Normal	13	100.0%	22	53.7%	0.01
	low grade fever	0	0.0%	18	43.9%	
	high	0	0.0%	1	2.4%	
ISC stay days	1-5	9	81.8%	31	88.6%	0.338
	<10	0	0.0%	2	5.7%	
	>10	2	18.2%	2	5.7%	
Postoperative chest drain volume	<500 ml	12	100.0%	36	90.0%	0.522
	(500-1000) ml	0	0.0%	3	7.5%	
	>1000	0	0.0%	1	2.5%	
Noninvasive ventilation use	No	7	53.8%	29	70.7%	0.260
	Yes	6	46.2%	12	29.3%	
Inotrope postoperatively	No	6	46.2%	22	53.7%	0.637
	Yes	7	53.8%	19	46.3%	
Pao2 <70	No	11	84.6%	36	87.8%	1.00*
	Yes	2	15.4%	5	12.2%	

Table 10. Post- operative factors (scale variables)

Variable	Number of patients		p
	N=13	N=41	
	Control (non-delirium)	Cases (delirium)	
Total amount of midazolam /mg	.1±.1	.09±.091	0.947
Bolus doses of morphine/mg	.00±.000	1.17±.308	0.001
Length of stay in ICU-days	2.54±.978	1.47±.308	0.317
Hb	9.93±.426	9.70±.219	0.620
Sequential organ failure assessment score (SOFA)	4.85±.390	5.56±.191	0.083

Hyperactive subtype (A), Hypoactive subtype (B) and mixed incidence of delirium

Based on Meaghe criteria Patients were classified as

- if they had three or more of the following: hyper-vigilance, restlessness, fast or high speech, anger or irritability, companion unit, impatience, cohesive, swearing, singing, laughing, euphoria, wandering, light-hearted, distracting, nightmares, persistent thoughts.
- Hypoactive subtype (B) if they had four or more of the following: Unconsciousness, decreased vigilance, sparse or slow speech, drowsiness, decreased motor activity, stare, and apathy.
- Mixed subtype if they met the criteria for both (A) and (B)

Table (11) below shows the percentages and frequency of patients having Hyperactive or Hypoactive Delirium or mixed. 22(54.7%) of patients with delirium had subtype A, 11 (25.9%) had subtype B, and 6

(13%) had mixed. It means that the most common types of delirium is Hyperactive subtype (A).

Table 11: delirium incidence by type based on Meaghe criteria

Type	Categories	Percentage	Frequency
Hyperactive subtype (A)	Not of subtype A	45.3%	19
	Subtype A	54.7%	22
Hypoactive subtype(B)	Not of subtype B	74.1%	30
	Subtype B	25.9%	11
Subtype mixed	Not mixed	87.0%	35
	Mixed	13.0%	6

In table (12) a cross tabulation of being hyperactive, hypoactive delirium and a set of demographics; education, smoking status gender and marital status. Of those who was hyperactive about 65.5% were of tawjihi or less education compared to 34.5% of university education (p = 0.0617). The result indicates that low education was a predisposing factor for hyperactive delirium. About 41.4% were smokers compared to 58.6% none smokers (p= 0.2882), 69% were males compared to 31.0% females P = 0.0186. This result indicates that to be a male was a predisposing factor for hyperactive delirium, 96% were married, compared to 3.6% unmarried (P < 0.0001) and the ages mean of those hyperactive was 61 years comparing to 55years of non-hyperactive. while of those who were classified as hypoactive, about 64% were of tawjihi or less education, about 43% were smokers, about 71% were males, about 93% were married and the mean ages of those hypoactive was 62years comparing to 56 of non-hypoactive.

This means that the predisposing factors for hyperactive subtype (A) and hypoactive subtype (B) delirium are low education, smokers, to be male, to be married and be over 60 years old.

Table 12: Crosstab of demographics variables and being of hyperactive subtype (A) or hypoactive subtype (B)

Variable	Categories	Not subtype A	Subtype A	Not subtype B	Subtype B
Education	Tawjihi or less	(70.8%)	(65.5%)	(67.5%)	(64.3%)
	University	(29.2%)	(34.5%)	(32.5%)	(35.7%)5(
Smoking status	No	(37.5%)	(58.6%)	(47.5%)	(57.1%)
	Yes	(62.5%)	(41.4%)	(52.5%)	(42.9%)
Gender	Male	(70.8%)	(69.0%)	(67.5%)	(71.4%)
	Female	(29.2%)	(31.0%)	(32.5%)	(28.6%)
Marital status	Married	(91.7%)	(96.4%)	(94.9%)	(92.9%)
	Unmarried	(8.3%)	(3.6%)	(5.1%)	(7.1%)
Age (Mean)		55	61	56	62

Chapter Five
Discussion

Discussion

This chapter provides a discussion and clarification of the study outcomes in regard to the occurrence of delirium and predisposing as well as precipitating factors of delirium in patients undergoing on pump cardiac surgery.

The underlying pathophysiology of delirium is not known, some of the preeminent hypotheses are similar to those proposed for neurodegenerative processes such as Alzheimer's disease and other kinds of dementia. One is pivotal cholinergic deficiency that performs a basic vulnerability that predisposes persons to delirium (Hshieh et al., 2008). Adding is inflammation, which can show a paramount role both as a predisposition factor in the mode of CNS inflammation and a precipitating factor from systemic inflammation, such as infection (Maclullich et al., 2008). It is thus essential that in the majority of studies, the most persistent risk for postoperative delirium is by then existing cognitive impairment and this result is analogous to formerly published studies (Bitsch et al., 2004; Dasgupta and Dumbrell, 2006).

A diversity of risk factors have been suggested to origin to post-operative delirium after cardiac surgery. Risk factors were here splitter into predisposing and precipitating variables. The predisposing factors address risks acknowledged in advance of surgery. The precipitating factors reverse intraoperative and initial postoperative events, and if known, might be monitored to avert post-operative delirium.

This study reaches the following results:

- No relation could be detected between delirium and the demographic variables.
- No relation could be detected between delirium and the pre-operative factors given that highlighted variables such as cardiogenic shock, depression and chemotherapeutic agent could not be tested because none of the patients experienced such a condition.
- Among the intraoperative factors, the total amount of midazolam and morphine use of a significant association between the control group and the cases group for the favor of control group
- Among the intraoperative factors, the total amount of Atropine use of a significant association between the control group and the cases group for the favor of control group
- Amongst post-operative factors low grade fever, bolus doses of morphine and SOFA were of significant relations with developing delirium for the favor of control group.

In this comprehensive analysis of 54 consecutive patients undergoing cardiac surgery, The greatest incidence of delirium was 75.9% (41 patients) of the targeted sample developed delirium in the ICU at the same day of surgery, and 9 (35.2%) in the first day of surgery, the percentage continued to drop until it reached 3.7% (2 patients) in the second and third day of surgery.

This recurrence was more to published data conducted by McPherson, et al., (2013) showed that the incidence of delirium in the cardiovascular intensive care unit (CVICU) was 26% and also greater than previous report by Rudolph, et al., (2009) who declared that delirium occurred in 63 (52%) of the cohort patients, and exceeding previous report by Chang, et al., (2014) declared that the prevalence of postoperative delirium was 41.7%.

In the current study, of the patients with delirium, 26.8% of patients experienced hypoactive delirium, 52.5% with hyperactive delirium and 12% had mixed delirium. These results are partially in agreement with the study results of McPherson et al (2014) who was shown that of the patients with delirium, 91% of patients experienced hypoactive delirium, 4% with hyperactive delirium and 6% had mixed delirium

The delirium percentage in our study located in the higher part of published reports. There are several causes for this. First, our study has utelized CAM-ICU delirium detection methods, including a standardized evaluation delivered daily. This standard delirium tool includes assessments that may not be recognized in a routine clinical interview. The incidence of delirium following cardiac surgery diverges highly (2-73%) (Sockalingam, et al., 2005).

Studies utelizing a Standardized Assessment Tool as in Santos, et al., (2004), have shown greaterr incidence of delirium 74 (33.6%) patients than studies that evaluate delirium via blueprint examination or nursing report (Norkiene et al., 2007). In Norkeine study, delirium was found in 42 (3.07%) patients.

Predisposing factors (present prior to surgery) (Preoperative risk factor).

Rudolph et al (2009) determine four preoperative factors that were independently correlate with postoperative delirium: defective cognition, depressive symptoms, preceding stroke or TIA and aberrant albumin. These risk factors were not compelling in the current study between groups of patients with and without delirium. None of the other pretend variables were preoperatively significant correlated with delirium

Older age estimates as a risk factor for postoperative delirium (Plaschke, et al 2010; Schoen, et al., 2011) and the current study enrolled patients 18-60, mean (SD) 57.72±1.329 which is younger than other studies of delirium after cardiac surgery.

A study performed by Chang, et al (2008), who showed that the factors that more extensive in patients with delirium than in patients without delirium were elder age, little educational level, unmarried, a history of psychological disturbances, diabetes mellitus, a history of stroke or renal disease, despondent left ventricular function, preoperative atrial

fibrillation or cardiogenic shock. The results of the current study are not in an agreement with Chang et al study in all variables that mentioned above.

In the current study, preoperative statin was not a predisposing factor of delirium. This finding was in align with some studies that shown that the influence of preoperative statin use on the outset of delirium following cardiac surgery have incensed contradictory results: one of the studies especially concentrate on preoperative statin use showed that it was defensive opposing delirium (Katznelson, et al., 2009), and two studies did not find a statistically significant relationship between lipid diminished agent and delirium (Hudetz, et al., 2009; Burkhart, et al., 2010).On the contrary, our finding is not compatible with a study conducted by Redelmeier, et al., (2008) who showed that statin was anticipating of delirium.

Precipitating factors (occur intraoperative and after surgery),

In the current study, the finding that the duration of anesthesia was not combine with delirium. This finding was not at the same line with the study results performed by Rudolph et al. (2010) who was shown that the duration of anesthesia was combined with delirium.

In our appraisal of delirium prevalence, There were significant differences between cases and controls in the amounts of midazolam performed intra-operatively, total amount of Midazolam was significantly greater in the control group (non-delirium) 3.31±0.398, compared to the case (delirium) 2.41±.135 (p= .051). The results were shown that

administration of Midazolam intraoperatively was not a precipitating factor of delirium. Contrariwise, McPherson et al. (2014) showed that benzodiazepine usage at admission was independently predictive of a 3-fold inclined risk of an incident of CVICU delirium.

In the current study with view to intra-operative variables: CPB duration, MAP, hemoglobin level, body temperature, noradrenaline requirement, and transfusion of RBCs and platelets were not significant between the control and cases groups. These results of the current study are not in accordance with the study managed by Rudiger et al. (2016) who was demonstrated that lengthy CPB duration, low MAP, low hemoglobin level, low body temperature, high noradrenaline requirement, and administration of RBCs and platelets were significant intra-operative risk factors. In the multivariate analysis, only platelet handling are remained independent, suggesting that platelets administration are an independent risk factor for amelioration of delirium in the ICU.

In the current study, hemodynamic status was not combined with the amelioration of delirium on consecutive days in ICU. These results are in concession with the study results attended by McPherson et al. (2014).

In the present study, there was no significant association between hemoglobin intra-operatively and the existence of delirium. These results are rational with study results performed by Bakker et al. (2012) and Schoen et al., (2011).

A positive association between low hemoglobin levels and delirium was established in some studies (Kazmierski et al., 2010; Tully et al., 2010). Research in rats revealed that blood administration principally and free hemoglobin in particular increment interleukin 6 levels and matter neuro-inflammation with consequent cognitive flawed (Tan et al., 2015).

In the current study there were no significant differences between the patients with or without delirium respecting C-reactive protein and leucocyte, these findings are not in accordance with the study results performed by Rudiger et al (2016) showed that post-operative leukocyte counts and C-reactive protein levels were considerably but significantly greater on ICU admission, which could demonstrate a role of systemic inflammation in the evolution of delirium. This hypothesis is approved by earlier work describing increased levels of cytokines such as interleukin 6 in patients with delirium (van den Boogaard, et al., 2011; Skrobik, et al., 2013).

In the present study, there were no significant differences between patients with or without delirium respecting the rate of creatinine postoperatively. These results are not in line with the study results performed by Rudiger et al. (2016) showed higher creatinine rate on ICU days 1 and 2 and more frequent use of continuous venovous hemodialysis in patients with delirium indicates a relationship between postoperative renal failure and delirium, as previously depicted by others (Mariscalco et al., 2012). The determinative systematic review by Gosselt et al. (2015)

expressed moderate evidence for acquaintance between postoperative renal failure and advancement of delirium.

In a study of Chang, et al., (2008) to investigate the predictive risk factors for postoperative delirium, the results showed that postoperative hematocrit less than 30%, postoperative cardiogenic shock, postoperative hypoalbuminemia and postoperative acute infection was independent, significant predictors of postoperative delirium. Low hematocrit can cause inadequate delivery of oxygen to the brain, culminating in organ dysfunction and delirium (Marcantonio, et al 1998). Postoperative cardiogenic shock also amalgamate brain circulation and blood oxygen carrying capacity (McKhann, 2002). Hypoalbuminemia can induced by poor nutrition or metabolic disorder, principally in critically ill patients.

Low plasma levels of albumin decreases colloidal oncotic pressure, somewhat because albumin shifts away vascular space to the interstitial space during acute inflammation, advanced to organ failure delirium. Acute infection or sepsis presumably constitutes a reliable high risk of acute confusion. All of the attributes that mentioned above could be compelling with the current study results in regard to the patient with delirium have significantly low grade fever compared to none delirium patients and patients with delirium have higher Sequential Organ Failure Assessment (SOFA) Score in comparison to patients with no delirium.

In the current study, there was no significant difference between the control and cases groups in regards to Fentanyl. Fentanyl attained during the operation confers to the median dose in milligrams per patient without normalizing to body weight. This finding is appropriate with the study results in a randomized controlled study by Gamberini et al. (2009) had analyzed the amount of fentanyl given during the operation according to the median dose in milligrams per patient without normalizing to body weight and this declined to show a significant influence of Fentanyl dose on delirium. Another study by Hudetz et al. (2009) did not evaluate the dose of fentanyl per kg body weight, and they did not find a significant boost in the incidence of delirium with expanding doses.

The anesthetic ketamine is broadly regarded as a "dissociative" drug and has often been joined to emergence delirium (Lohit, et al., 2011). In the current study, there was no significant difference between control and cases groups of delirium as regards the use of ketamine intraoperatively. However, it has been remarkably demonstrated in a prospective randomized study by Hudetz et al. to decrease the incidence of postoperative delirium following cardiac surgery. Patients were randomized to get either a 0.5 mg / kg intravenous dose of ketamine or placebo and all patients obtained fentanyl and etomidate for anesthetic induction. Patients who had received ketamine during anesthesia induction had a delirium incidence almost thirteen times lower than in patients getting placebo ($p = 0.01$) (Hudetz et al., 2009). There was also a association between ketamine usage and the levels of C-reactive protein

(CRP) in patients, by which patients acquiring ketamine also had reduce CRP levels ($p < 0.05$) (Hudetz et al., 2009). This led Hudetz et al. to presuppose that as it may be ketamine gave a neuroprotective effect by adjutant as an anti-inflammatory agent in the postoperative period to avert cytokines from intrusive with brain metabolism.

Postoperative precipitating factors

In the current study, the Precipitating factors envisaged for evolved delirium constituted use of atropine, the number of patients who were given atropine is higher in control group 3(23.1%) compared to the case group 1(2.4%), ($p = 0.062$). This finding is in agreement with two proposed observation studies with patient samples of similar average ages went through CABG, conducted by Tan et al. (2010) and Tully et al. (2015). These two studies assisted the association between preoperative anticholinergic drug usage and postoperative delirium and did not find an association between anticholinergic and delirium.

On the other hand, O'Hare, et al., (1997) showed that anticholinergics, such as atropine, have long been proposed to outgrowth delirium-like conditions in humans.

Koster et al. (2008), showed that preoperative usage of opioids was not combined with postoperative delirium following cardiac surgery ($p = 1.00$). In our study showed that intra-operative usage of opioids was not combined with postoperative delirium following cardiac surgery but post-operative usage of opioids was significantly associated with postoperative

delirium ensuing cardiac surgery. On the contrary, in a prospective study showed that no statistically significant relationship between the averages of morphine dose expended over 3 postoperative days and the occurrence of delirium [Burkhart, et al., 2010)]. Hudetz et al. (2009) could not encounter any association between the amounts of morphine utilized on the day of surgery, the amount of morphine expended on postoperative day 1 or the percentage of patients taking morphine postoperatively, with the existence of delirium

In the current study, SOFA score was higher in the cases group 5.56±.191 compared to the control group 4.85±.390, (p=0.083). Unexplored organ dysfunctions should increase the possibility of an underlying infection being the provocateur to delirium. Rasulo, et al., (2017) stated that re-evaluate criteria for sepsis, with a extensive base of constituents, should also contemplate delirium to refine the criteria for sepsis.

Expanding experimental and clinical evidence is accessible to suggest that trauma, infection or surgery may lead to heightened production of pro-inflammatory cytokines (Bekker, et al., 2003) which may cause delirium in receptive individuals (Koster, et al., 2008). Peripheral secreted cytokines may aggravate exaggerated responses from microglia and thereby cause severe inflammation in brain (Nishtala, et al., 2009). Proinflammatory cytokines can significantly influence the synthesis or discharge of acetylcholine, dopamine, norepinephrine and 5-HT, thereby intrusive with neuronal communication (Chew, et al., 2008), and they can

also produce a direct neurotoxic effect (Carnahan, et al., 2006). Moreover, proinflammatory cytokine levels have been demonstrated to increase in patients with delirium (Vaughan, et al., 1999; Mukai,, et al., 2003; Marcantonio, et al., 2003).

The existence of low-grade inflammation combined with chronic neurodegenerative divergence in the brain in patients with dementia may interpret why these individuals are at elevated risk of delirium.

In the current study, there was no significant difference of postoperative delirium respecting the mean of length of stay (LOS) in ICU between the control group (patients without delirium) 2.54±.978 days and cases group (patients with delirium (1.47±.308 (p=0.317). The current study discovery is not consistent with the study result conducted by Brown, et al., (2014) showed that the median LOS ICU was higher in patients with delirium (75.6 hours, IQR 43.6-136.8) compared to patients without delirium (29.7 hours, IQR 21.7-46.0; P = 0.002).

Conclusions

A compelling percentage of cardiac surgical patients encountered delirium in ICU, broadly in its hyperactive form. Few modifiable risk factors have been determined that could lower the probability of post cardiac surgical ICU delirium. One should contemplate the use of midazolam, morphine and atropine intra-operative as protective drugs for postoperative delirium. Low and high grade fever, postoperative morphine usage and augmenting of SOFA score are precipitating factors for postoperative delirium.

Strengths and limitations of the current study

We completed a detailed, ultimate evaluation of delirium with a standardized bedside instrument and assessed several predisposing and precipitating factors. We were also adept to study the delirium motor subtypes in a companion of surgical cardiac patients, although we used an efficient approach to using RASS along with the CAM-ICU to describe these motor subtypes.

Delirium appraisal occurred only once a day and only when patients were in CCU; given the waver rate of delirium, it is conceivable that we may have undervalued the presence of delirium. It is possible that alternative risk factors might have been vanished. We consider that this study flourishes the knowledge of delirium and its risk factors in heart surgery patients. The present study is limited by the number of patients included. Further research is needed with a larger sample.

Recommendation

Delirium should be evaluated personally in the ICU following cardiac surgery by competent nurses on daily bases using the endorsed confusion assessment method (CAM-ICU). Because delirium is likely preventable, governed trial protocols for high-risk patients can be an essential strategy for quality improvement of care.

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Appendix 1

Instrument:

The researchers had utilized this short CAM- ICU.

SHORT CONFUSION ASSESSMENT METHOD (SHORT CAM) WORKSHEET (**Ely, et al 2001, Francis**, et al, 2001)

EVALUATOR: **DATE:**

I. ACUTE ONSET AND FLUCTUATING COURSE **BOX 1**

Is there evidence of an acute change in mental status from the patient's baseline?

No ____ Yes ____

a) Did the (abnormal) behavior fluctuate during the day, that is tend to come and go or increase and decrease in severity?

No _____ Yes ___

II. INATTENTION

Did the patient have difficulty focusing attention, for example, being easily distractible or having difficulty keeping track of what was being said?

III. DISORGANIZED THINKING

Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?

BOX 2

No _____ Yes _____

IV. ALTERED LEVEL OF CONSCIOUSNESS

Overall, how would you rate the patient's level of consciousness?

--- Alert (normal)

--- Vigilant (hyperalert)

--- Lethargic (drowsy, easily aroused)

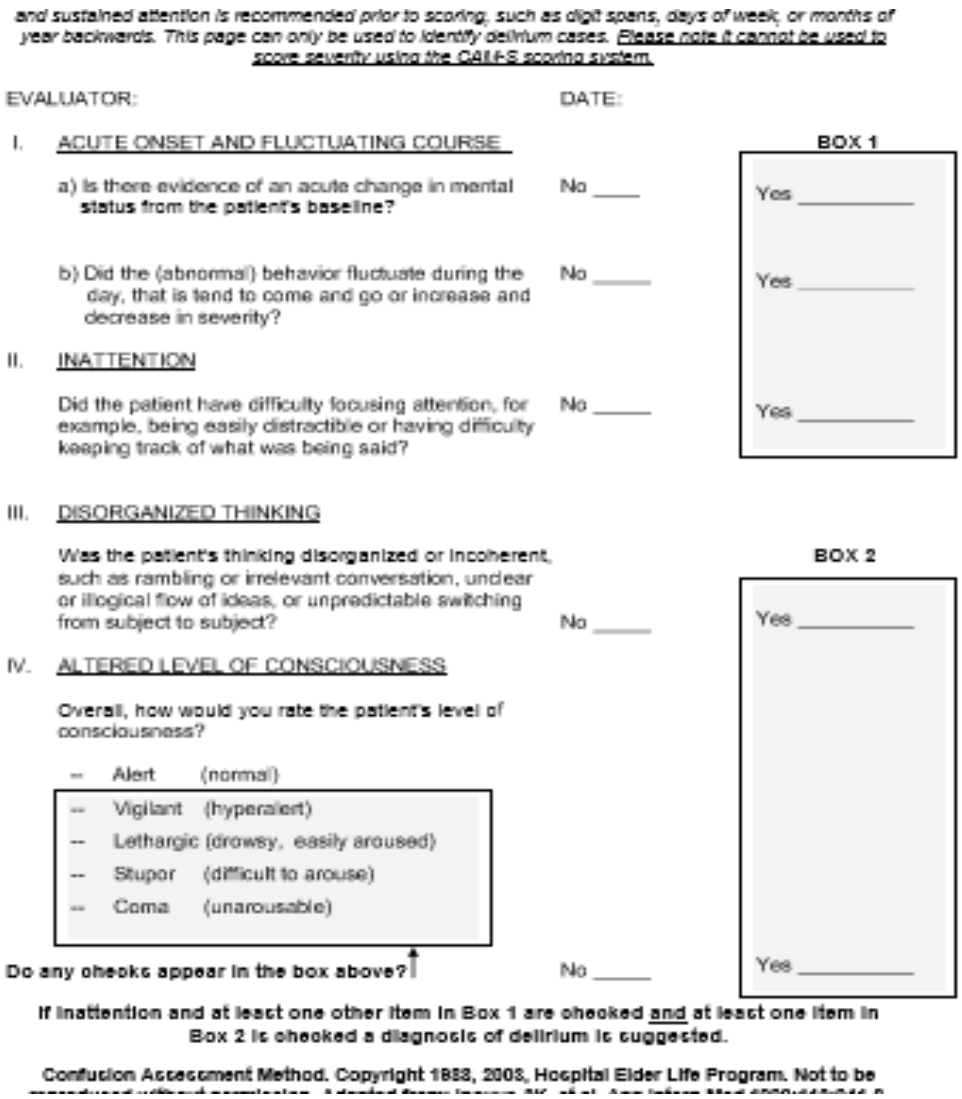
--- Stupor (difficult to arouse)

--- Coma (unarousable)

Do any checks appear in the box above? No _____ Yes _____

If Inattention and at least one other item in Box 1 is checked <u>and</u> at least one item in Box 2 is checked a diagnosis of delirium is suggested.

Confusion Assessment Method. Copyright 1988, 2003, Hospital Elder Life Program. Not to be reproduced without permission. Adapted from: Inouye SK, et al. Ann Intern Med.1990; 113:941-8.



and sustained attention is recommended prior to scoring, such as digit spans, days of week, or months of year backwards. This page can only be used to identify delirium cases. <u>Please note it cannot be used to score severity using the CAM-S scoring system.</u>

EVALUATOR: DATE:

I. <u>ACUTE ONSET AND FLUCTUATING COURSE</u>

BOX 1

a) Is there evidence of an acute change in mental status from the patient's baseline? No ____ Yes _____

b) Did the (abnormal) behavior fluctuate during the day, that is tend to come and go or increase and decrease in severity? No _____ Yes _____

II. <u>INATTENTION</u>

Did the patient have difficulty focusing attention, for example, being easily distractible or having difficulty keeping track of what was being said? No _____ Yes _____

III. <u>DISORGANIZED THINKING</u>

BOX 2

Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject? No _____ Yes _____

IV. <u>ALTERED LEVEL OF CONSCIOUSNESS</u>

Overall, how would you rate the patient's level of consciousness?

-- Alert (normal)
-- Vigilant (hyperalert)
-- Lethargic (drowsy, easily aroused)
-- Stupor (difficult to arouse)
-- Coma (unarousable)

Do any checks appear in the box above? No _____ Yes _____

If inattention and at least one other item in Box 1 are checked <u>and</u> at least one item in Box 2 is checked a diagnosis of delirium is suggested.

Confusion Assessment Method. Copyright 1988, 2003, Hospital Elder Life Program. Not to be

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.(4)

> **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 (Glascow 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**

Appendix 2

Data Sheet

Preoperative phase

Name		Gender	□ Male □ Femalr
Education	□ Tawjihi or less □ university	Age	
Smoking	□ Yes No□	Marital status	Unmarried□ □ Married
Preoperative diseases			
Valvular heart disease	□ Yes No□	Diabetes	Yes□ No□
Coronary artery disease	□ Yes No□	Renal dysfunctio	Yes□ No□
hypertention	□ Yes □ No	Pulmonary arterial hypertension	□ Yes □ No
Thyroid disease	□ Yes □ No	Depression,	□ Yes □ No
LVEF less than 30	Yes□ □ No	Atrial fibrillation	Yes□ □ No
Hearing impairment	□ Yes No□	Visual impairment	□ Yes □ No
Cadiogenic shoc	Yes□ No□	NYHA 3 or 4,	□ Yes □ No
Carotid artery disease	Yes	Preoperative statin use	Yes
Medications with psychoactive potential such as benzodiazepines	□ Yes No□	Use of corticosteroids	□ Yes No□
Use of non-, steroidal antiinflammatory agents (NSAIDS),	□ Yes No□	Opiates use	Yes□ No□
Chemotherapeutic agent	□ Yes □ No		

Code Number: ----------

Paient name----------

Intra-operative phase

Total amount of midazolm/ mg		Total amount of ketamine/ mg	
Using of phenylephrine		Using of morphine/mg	
inotrope use	1. 2. 3. 4.	Total amount of propofol/mg	
Total amount of fentanyl/µg		Total amount of blood transfusion/unit	
Total amount of fresh frozen plasma/unit		Total amount of platelets	
cardiopulmonary bypass (CPB) time/ min		aortic cross-clamp time/min	
Extubation in OR	□ Yes □ No	Intra aorta baloon pump	□ Yes □ No
Temperature			

Coding Number----------

Name of the patient----------

Postoperative phase

Reoperation	□ Yes □ No		
Total amount of midazolam/mg		bolus doses of morphine/mg	
The total time on mechanical ventilation/hr	□ <12h □ 12-24h □ 25-48h □ 49-72h □ <3 days	Total doses of propofol/mg	
Atrial fibrilation	□ Yes □ No	fresh frozen plasma	□ Yes □ No
Blood transfusion	□ Yes □ No	Intra aortic baloong pump	□ Yes □ No
Platelet trasfusion	□ Yes □ No	bilirubin >2mg/dl	□ Yes □ No
Cadiogenic shoc	□ Yes □ No	Hb	
Postoperative infection	□ Yes □ No	PaO2 <70	
Na >140, mEq	□ Yes □ No	use of atropine	□ Yes □ No
Prolonged hypotension	□ Yes □ No	postoperative tachycardia	□ Yes □ No
sleep deprivation	□ Yes □ No	Hematocrit <30	□ Yes □ No
Postoperative pain VAS ≥4	□ Yes □ No	postoperative chest drain volume	ml500< 1000-500 >1000

Creatinine >2 mg/dl	□ Yes □ No	noneinvasive ventilation use	□ Yes □ No
Sequential organ failure assessment score (SOFA)		Inotrop postoperatively	□ Yes □ No
Temperature	□ Normal □ Low grade fever □ High	Sleep deprivation	
ICU stay (days)	5-1 10-6 <10		

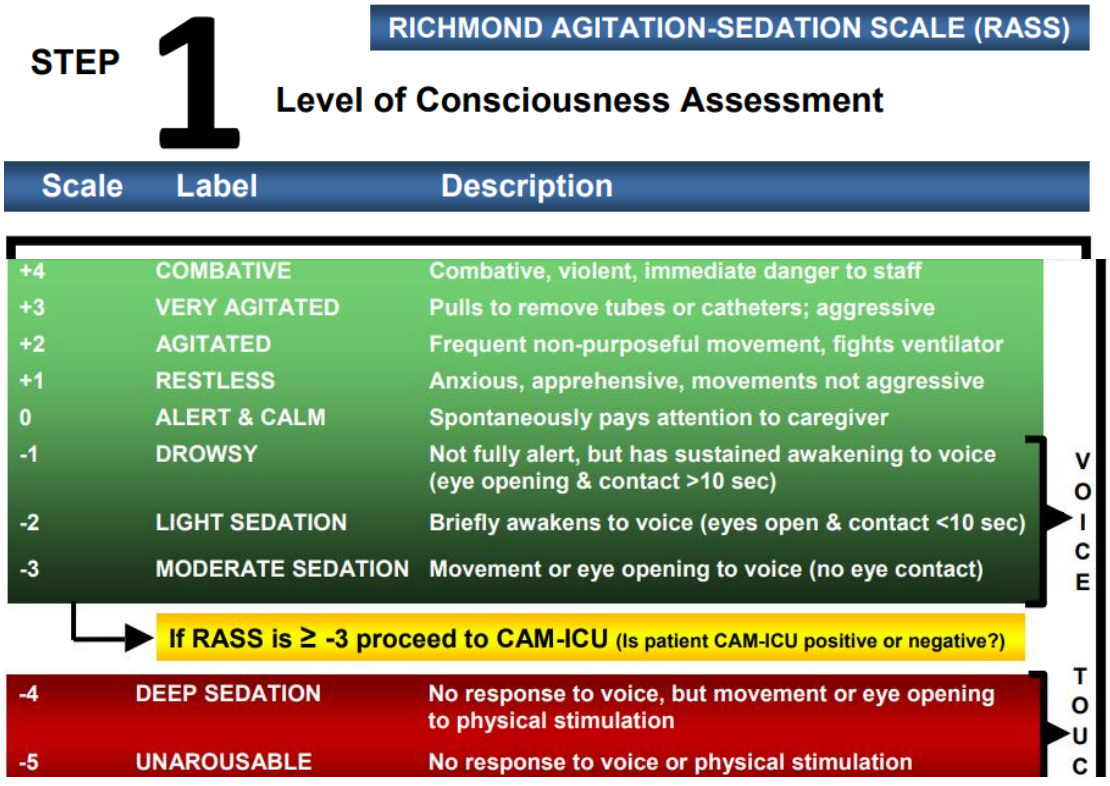
hyperactive" subtype (A)	
يقظة مفرطة Hypervigilanc	□ Yes □ No
Restlessness	□ Yes □ No
Fast or loud speech	□ Yes □ No
Anger or irritability	□ Yes □ No
Combativeness حالة الاشتباك في قتال	□ Yes □ No
Impatience	□ Yes □ No
Uncooperativeness	□ Yes □ No
Swearing	□ Yes □ No
Singing	□ Yes □ No
Laughing	□ Yes □ No
Euphoria intense excitement and happiness	□Yes □ No
Wandering شرود	□ Yes □ No
Easy startling مفزع	□ Yes □ No
التشتت Distractibility	□ Yes □ No
Nightmares	□ Yes □ No
الأفكار المستمرة Persistent thoughts	□ Yes □ No

hypoactive subtype (B) delirium	
Unawareness	□ Yes □ No
Decreased alertness	□ Yes □ No
خطاب متفرق أو بطيء Sparse or slow speech	□Yes □ No
كسل Lethargy	□ Yes □ No
Decreased motor activity	□ Yes □ No
يحدقStaring	□ Yes □ No
لا مبالاة Apathy	□ Yes □ No

Appendix 3

Richmond Agitation Sedation Scale (RASS) *

Score	Term	Description
+4	Combative	Overtly combative, violent, immediate danger to staff
+3	Very agitated	Pulls or removes tube(s) or catheter(s); aggressive
+2	Agitated	Frequent non-purposeful movement, fights ventilator
+1	Restless	Anxious but movements not aggressive vigorous
0	Alert and calm	
-1	Drowsy	Not fully alert, but has sustained awakening (eye-opening/eye contact) to *voice* **(>10sec)**
-2	Light sedation	Briefly awakens with eye contact to *voice* **(<10 seconds)**
-3	Moderate sedation	Movement or eye opening to *voice* **(but no eye contact)**
-4	Deep sedation	No response to voice, but movement or eye opening to *physical* stimulation
-5	Unarousable	No response to *voice or physical* stimulation



Score	Term	Description
+4	Combative	Overly combative or violent and an immediate danger to staff
+3	Very agitated	Pulls on or removes tube(s) or catheter(s) or has aggressive behavior toward staff
+2	Agitated	Frequent nonpurposeful movement or patient ventilator dyssynchrony
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	
−1	Drowsy	Not fully alert but has sustained (>10 s) awakenings, with eye contact, to voice
−2	Light sedation	Briefly (<10 s) awakens with eye contact to voice
−3	Moderate sedation	Any movement (but no eye contact) to voice
–4	Deep sedation	No response to voice, but any movement to physical stimuli
−5	Unarousable	No response to voice or physical stimuli

Procedure:

جامعة النجاح الوطنية

كلية الدراسات العليا

التغيرات الفيسيولوجية المرضية والتدخلات العلاجية أثناء العملية للمرضى الذين يخضعون لعملية القلب المفتوح باستخدام مضخة جهاز القلب والرئة قد تكون عوامل خطورة لتطوير الهذيان بعد العملية الجراحية: دراسة إستطلاعية

إعداد

عبد الله ابراهيم حلاحله

إشراف

د. عايدة القيسي

د. وائل صدقة

قدمت هذه الأطروحة استكمالاً لمتطلبات الحصول على درجة الماجستير في العناية المكثفة، بكلية الدراسات العليا في جامعة النجاح الوطنية، نابلس- فلسطين.

2019

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الملخص

المقدمة: تعتبر حالة الاهتياج الناتجة عن عمليات القلب من المضاعفات الشائعة في وحدات العناية المكثفة الخاصة بأمراض القلب والأوعية الدموية حيث تشير تقديرات الحوادث بهذا الخصوص إلى أن 2-72% من هذه الحالات هي متلازمة عضوية حادة تتميز بالغفلة وعدم التكيف بالإضافة إلى تلف في واضطراب في حالة الوعي الإدراكي لدى المصاب. ومن خصائص هذا النوع من الاضطراب والذي يظهر بعد العمليات أن يتميز بنسبة مختلفة ويمكن له أن يرتبط إما بزيادة النشاط النفسحركي . وهذا النوع من الاهتياج يتميز عن غيره من الأنواع الأخرى نتيجة لأسباب منها: يمتلك الخاضعون للعمليات الجراحية المختلفة مظاهر علاجية مختلفة، وتتطلب جراحاتهم أساليب تخدير مختلفة وبالتالي ستختلف المنبهات الدوائية للاهتياج اعتماداً على نوع العملية، ويتطلب استخدام مجرى التنفس القلبي في جراحات القلب اعتبارات خاصة بسبب أن استخداماتها ترتبط بتأثيرات ما بعد العملية الجراحية على وظيفة الناقلات العصبية والزيادة في حالة الاهتياج. وفي هذا الصدد أظهرت الدراسات أن التنبؤات بحالات الاهتياج تظهر بأشكال مختلفة اعتماداً على نوع العملية وعلى مستويات المؤشرات البيولوجية لهذه الحالة. كما ان التعرف على عوامل الخطورة ضروري وذلك للنتائج الإيجابية للعملية الجراحية.

الهدف: تهدف هذه الدراسة إلى التعرف إلى إذا ما كانت إجراءات ما بعد العمليات الجراحية والتدخلات العلاجية تؤثر على مخاطر التهيج ما بعد العمليات الجراحية عند مرضى القلب في وحدات العناية المكثفة، كذلك تهدف إلى تحديد حوادث التهيج وعوامل الخطورة فيها عند هؤلاء المرضى.

الطريقة والإجراءات: استخدم الباحث المنهج الوصفي التحليلي من خلال تطبيقه على ثلاث وحدات جراحة القلب في ثلاثة مستشفيات فلسطينية حيث تشكلت عينة الدراسة من 60 مريضاً تم إدخالهم إلى العناية المكثفة الخاصة بجراحة القلب، وقد تم إعداد تقرير طبي مفصل من أجل جمع البيانات من المرضى وذلك لتحديد تأثيرات المتغيرات على حالة الاهتياج ما قبل، وأثناء وما بعد العملية، ومن ثم تم تصوير جميع أفراد العينة باستخدام اختبارات (RASS وCAM- ICU) مرة يومياً ومن ثم تم اعتبار من حصل على فحوصات ايجابية حالات بينما تم اعتبار الآخرين مجموعة ضابطة.

النتائج: بلغت نسبة المرضى الذين تطورت لديهم حالة الاهتياج 75.9% أي 54/41 من عينة الدراسة وقد استمرت هذه النسبة بالهبوط حتى وصلت إلى 3.7% أي مريضين اثنين. لم يلاحظ وجود أي علاقة بين تربط حالة الاهتياج بالمتغيرات الديمغرافية (التعليم، والتدخين، والنوع الاجتماعي بالإضافة إلى العمر)، كذلك لم تكن هناك علاقة بين حالة الاهتياج وعوامل ما قبل العملية. أظهرت النتائج أنه وخلال العملية بلغت نسبة مادة الميدازولم/ ملغم في المجموعة الضابطة بمتوسط قدره 3.31 وإنحراف 0.398 مقارنة مع متوسط 2.41 وإنحراف 0.135 في مجموعة الاهتياج عند مستوى دلالة (0.051) وفترة ثقة 0.95 . وأظهرت النتائج أيضاً أن من لم يعانوا من الاهتياج بعد إجراء العملية لديهم نسبة أعلى من مادة الميدازولم. وأن هناك فروق دالة إحصائيا عند فترة ثقة 0.95 في مجموع الميروفين/ مليغرام في المجموعة الضابطة التي لا يوجد بها حالة اهتياج بمتوسط 8.85 وانحراف 1.04 مقارنة بمجموعة الاهتياج والتي جائت بمتوسط 7.93 وانحراف 0.45 . وأظهرت النتائج أيضاً أن تم إعطاؤهم موريفين أكثر أثناء العملية كانوا أكثر حظاً في عدم تطور حالة الاهتياج لديهم بعد خضوعهم للعملية الجراحية. أما بالنسبة للمتغير الذي وجد له علاقة دالة إحصائياً فهو استخدام مادة الأتروبين حيث وجد ان من استخدم أتروبين كانوا أقل احتمالية وبصورة دالة لتطور حالة الاهتياج لديهم. كذلك وجد في المجموعة الضابطة (بدون وجود حالة اهتياج) أن 3 مرضى (23.1% تلقوا اتروبين مقارنة مع مريض واحد (2.4%) بمستوى دلالة 0.062 من مجموعة الاهتياج. وبالنسبة لدرجة الحرارة وعند مستوى ثقة 95% فإن المرضى الذين كانت حرارتهم مرتفعة او متدنية وعددهم 19 (46.3%) في مجموعة الاهتياج مقارنة مع 0 (0.0%) في المجموعة الضابطة وبمستوى دلالة (0.01) كانوا إقل احتمالية لتطور

الحالة وبصورة دالة إحصائياً وهذه النتيجة تشير إلى أن درجة الحرارة المتدنية أو المرتفعة في ما بعد العملية هي عامل مفاجئ بالنسبة لحالة الاهتياج. أما بالنسبة لجرعات المضغ من المورفين/ملغم عند درجة ثقة95% في المجموعة الضابطة (بدون اهتياج) فقد جاءت بمتوسط حسابي 0.00 وانحراف معياري 0.00 مقارنة مع متوسط حسابي 1.17 وإنحراف معياري 0.308 ومستوى دلالة 0.001 في مجموعة الاهتياج، وأن المرضى التي تلقوا مورفين كانوا أكثر احتمالية وبصورة دالة إحصائياً لتطور الاحتياج لديهم في فترة ما بعد العملية الجراحية. واستناداً إلى درجة تقييم تتابع فشل الأعضاء عند درجة ثقة 59% فإن الذين كانت لهم درجة أعلى في مجموعة الاهتياج (بوسط حسابي 5.56 وإنحراف معياري 0.191 كأنوا أكثر احتمالية تطوير اهتياج مقارنة مع المجموعة الضابطة (بدون حالة الاهتياج) والتي جائت بمتوسط حسابي 4.85 وإنحراف معياري 0.390 ومستوى دلالة 0.083، وهذه النتيجة تشير إلى أن ارتفاع درجة تقييم تتابع فشل الأعضاء يعتبر عامل مفاجئ. إضافة لذلك شوهد نوع الاهتياج الزائد في 22 من 41 من المرضى (بنسبة مئوية بلغت 54.7%) بينما 11 من 41 (25.9%) من المرضى كانت لديهم حالة اهتياج زائدة إضافة إلى أن 6 من 41 من المرضى (13.0%) لديهم حالة مختلطة من الاهتياج.