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Research Article

Intraoperative Pathophysiological Changes and Therapeutic Interventions in Patients Undergoing On-pump Cardiac Surgery May be Risk Factors for the Development of Post-operative Delirium in the Cardiac Intensive Care Unit: A Prospective Observational Study

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Abstract

Introduction: Delirium after cardiac surgery is a common complication in cardiovascular intensive care units. Estimated incidence rates are approximately 30% to 73%. Delirium is an acute organic syndrome characterized by inattention, disorientation, along with global cognitive impairment and disturbance in consciousness. Post-operative 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 Post-operative 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 Post-operative outcomes.

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Aim: The aims of this study are to investigate whether intra-operative events and therapeutic interventions affect the risk of Post-operative 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, intra-operative and post-operative 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±0.135 in delirium group, p= 0.051, (59% confidence level) and the result shows that those who did not suffer from delirium Post-operative 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±0.45 (p= 0.085), 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 Post-operative is a precipitating factor for delirium. Post-operatively, bolus doses of morphine/mg (95% confidence level) as in the control (not delirium) M(SD) 0.00±.000 compared to 1.17±0.308 in the delirium group, p= (0.001) those patients who received morphine where significantly more likely to develop delirium Post-operatively. Regarding the Sequential Organ Failure Assessment score (SOFA) (90% confidence level) as those patients who scored higher SOFA in the delirium group 5.56±0.191were more likely to develop delirium compared with control group (not delirium) 4.85±0.390, (p= 0.083). This result indicates that higher SOFA was a precipitating factor for

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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 Post-operative delirium. Low and high grade fever, Post-operative morphine usage and augmenting of SOFA score are precipitating factors for Post-operative delirium.

Keywords

Cardiac Surgery; Delirium; CAM-ICU; Cardiac Intensive Care Unit; Risk Factors

Introduction

Delirium is a prudent problem in cardiac surgery [1]. The occurrence of delirium endure to increase among cardiac surgery patients [2]. The occurrence of Post-operative delirium alter between 2% and 72% based on the type of surgery executed [3]. 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 [4].

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. Hypothermia upon entrance into the recovery room has also been expressed to be a risk factor for hypoactive onset [5].

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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), 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 [6]. 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.

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 [7] . 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 [8].

Aim of the Study

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

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Secondary Objectives

• To investigate whether intra-operative therapeutic interventions affect the risk of Post-operative 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 Post-operative delirium in cardiac surgery ICU patients

• There is a significant association at 0.10 level related to intra-operative therapeutic interventions and Post-operative 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 [9]. Delirium is mediated to be an independent risk factor for long-term hospital stay and 6-month mortality [10]. Further, Post-operative delirium has significant financial ramifications, which have been shown to be combined with 39% higher intensive care units and 31% higher hospital costs. Accordingly, investigate even if intraoperative changes and therapeutic interventions affect the risk of Post-operative 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.

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The Significance of the Study

Delirium is a prevailing and life-threatening condition of intensive care. Even with expanded research, Post-operative delirium is a problem that attend to long-term hospitalization, elevated costs and raised mortality. There are a lot of predisposing factors for Post-operative 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 [11].

Background

Delirium is an acute organic syndrome characterized by inattention, disorientation, along with global cognitive impairment and disturbance in consciousness [11]. Post-operative delirium is typically characterized by a varying rate and can be associated with either increased or decreased psychomotor activity [12]. In addition, delirium-experienced patients often experience significant disorders in the sleep wake cycle [13].

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 [14]. Under normal aging, there is a decrease in the amount of acetylcholine producing cells and as a result, less ACh 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 [15].

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 post-operative delirium to range between 2 and 72% [16]. Variability may be due to lack of standardization

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of Post-operative 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 [17]. Procedural risk factors include prolonged surgery and Cardiopulmonary Bypass (CPB) times, exposure to anesthesia, increased Post-operative transfusion requirements, Post-operative tachycardia or hypertension, atrial fibrillation, elevated blood urea and pneumonia [18].

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 [19]: 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 [20].

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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 [21]. If possible is repeated 19 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 [22]. Access to photos, images, Calendars, watches, newspapers, TV and radio help patients to relax and improve orientation. 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 [23]. 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 [24]. According to Meagher, there are more than 60% of intensive care patients who experience sleep problems [25]. 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 [26]. 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 [27]. Haloperidol is often used when the effect of the drug is rapid and has few anticholinergic drugs side effects [28]. Clinics have been invited to consider alternatives medical treatments due to the adverse side effects that haloperidol may cause, examples of extrapyramidal symptoms [29]. For heart patients, however, it should have in mind that haloperidol can cause ventricular arrhythmias, prolonged QT time and cardiac arrest [30]. A few years ago, dexmedetomidine was launched, one sedative drug to be used Post-operatively 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 and Maze, (2011) mean that dexmedetomidine causes less memory and allows for more natural sleep [31]. Propofol is also a drug commonly used in intensive care. Segatore, et al., (1998) believe that Propofol may be a useful preparation when Post-operative delirium is

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so serious that the patient's life is threatened [32]. Propofol can help to quickly get control of the situation but do not solve the basic problem.

ICU Delirium Risk Factors

Risk factors for delirium could be prorated into predisposing factors and precipitation factors [33]. 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.

Afonso, et al., (2010) constitute an anticipating design for delirium Post-operatively in one hundred and twelve heart surgery patients [34]. 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. Delirium Post-operatively 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 [32]. A Mini-Mental Status Examination (MMSE) was applied to assess the cognitive function of the patients before operation and medical charts were appraised [36]. 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.

The trial by Schoen, et al., (2011) intended to explore preoperative and intraoperative cerebral oxygen saturation and its incorporation with delirium Post-operatively in participants go through heart surgery [33]. 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.

Girard, et al., (2008) studied sedatives and analgesics as risk factors for participant’s transformation to delirium [34]. 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.

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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, pre-operative comorbidities and intra-operative variables and post-operative 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

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Data Collection

A detailed clinical data sheet form is created to gather relevant data to determine the effect of preoperative, intraoperative and Post-operative 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 Post-operative data. The data sheet was based on the results of previous studies [28-34].

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 Association (NYHA) Classification 3 or 4, pulmonary arterial hypertension, depression, arterial disease, preoperative [25].

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 Post-operative is noted.

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Post-operative 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, Post-operative tachycardia, Intra-Aortic Balloon Pump Use (IABP) and insomnia, hematocrit <30, total amount of midazolam, bolus doses of morphine, Post-operative pain rated using VAS , Post-operative chest drainage volume, non-invasive ventilation use, days spent in ICU, Sequential Organ Failure Assessment Score (SOFA), use of inotropic Post-operatively are noted.

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 Post-operative complications. 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 Post-operative 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.

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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.

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

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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.

Fig. 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.

Fig. 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.

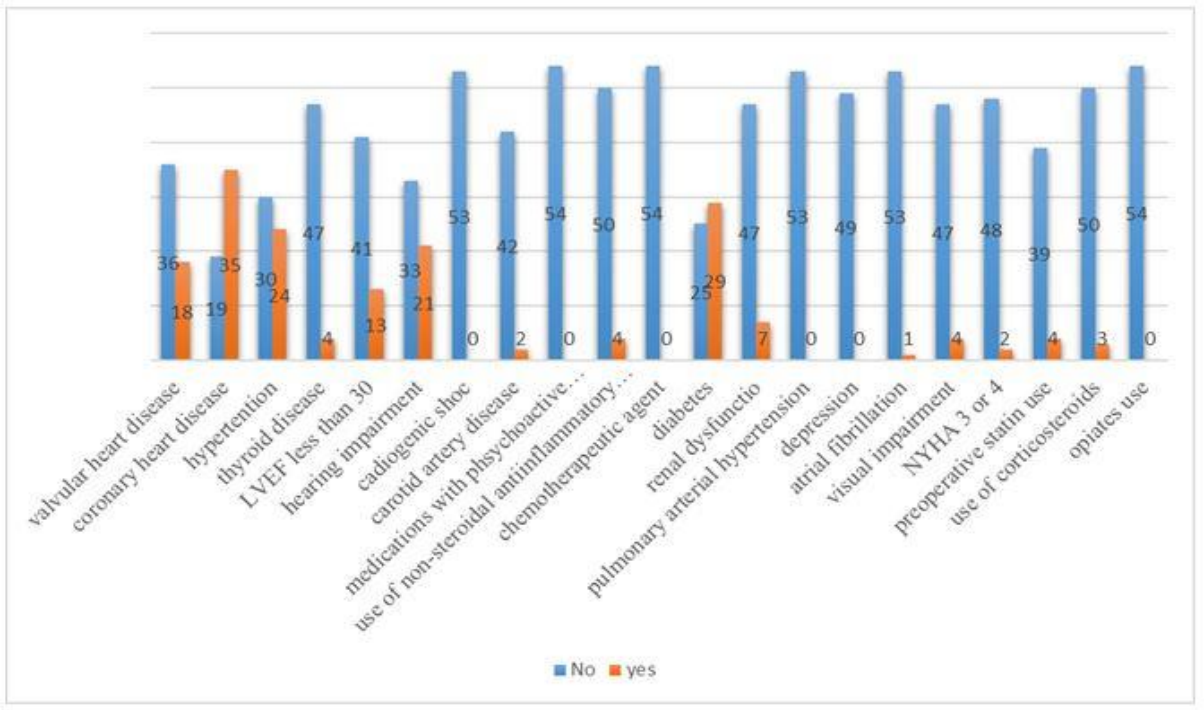

Figure 1: Descriptive statistics for pre-operative indicators (frequencies).

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Intra operative interventions

Fig. 2 shows intra operative interventions.

Fig. 2 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 (Fig. 2).

In Table 1, 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).

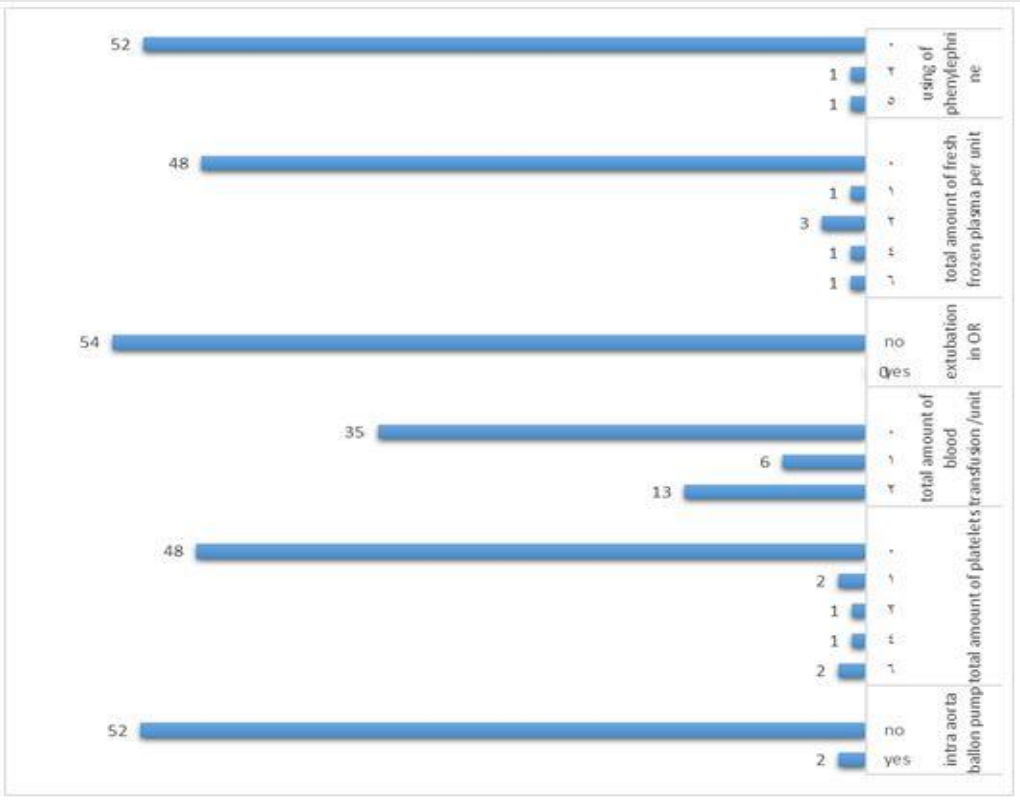

Figure 2: Intra operative interventions.

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Indicator	Mean	Std. Error of mean	Std. Deviation
Total amount of midazolam/mg	2.63	0.148	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	39.4	2.91	21.184
Total amount of morphine/mg	7.43	0.434	3.19
Total amount of propofol/mg	95.32	4.644	33.808
Aortic crossclamp time/min	96.5	4.151	30.506

Table 1: Shows the mean, standard error of mean and standard deviation for the scale interventions that has been done intraoperative.

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 2 below shows the percentages of patients who developed delirium after the operation and the three days following the operation.

As of the above table and Fig. 3, 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 2 shows the day when delirium started and when the symptoms disappeared, the Table 2 shows that almost half of the patients (46.3%) (25 patients).

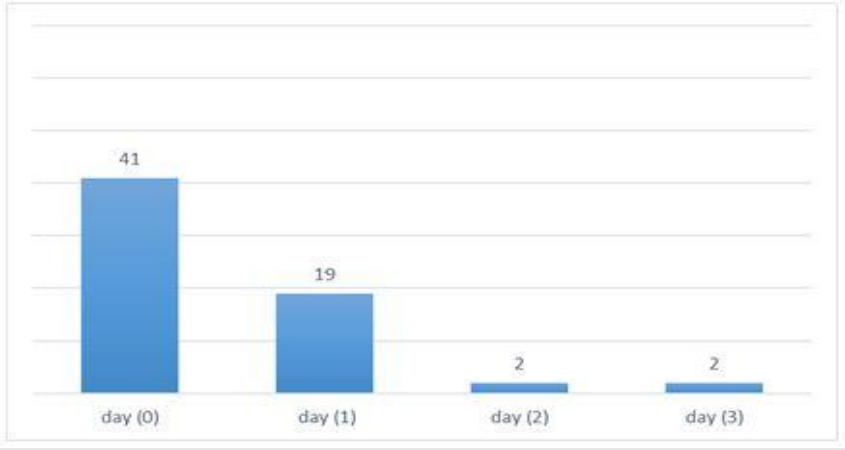

Figure 3: Incidence of post-delirium (counts).

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Status	Post-operative Day (0)	Post-operative Day (1)	Post-operative Day (2)	Post-operative Day (3)
Delirium%	75.90%	35.20%	3.70%	3.70%
Counts	41	19	2	2

Table 2: Incidence of post-operative delirium. Data is presented as counts and percentage.

Intra Operative Factors

t-test is used to test the scale variables as could be seen in Table 2, 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±0.135 in delirium group, p=0.051, (59% confidence level). 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±0.45 (p= 0.085), those who took more morphine/mg where more likely not to develop delirium after the surgery (Table 2). This result indicates that Morphine is a protective drug against delirium.

Variable	Number of Patients		P- value
	N=13	N=41	
	Control (nondelirium)	Cases (delirium)	
Total amount of midazolam/mg	3.31±0.398	2.41±0.135	0.051
Total amount fentanyl/mg	397.31±51.778	378.40±26.740	0.734
Cardiopulmonary Bypass (CPB) time/min	111.92±7.549	110.83±3.449	0.884
Temperature	33.38±0.65	32.36±0.30	0.117
Total amount of ketamine /mg	36.92±5.93	7.93±0.446	0.633
Total amount of morphine/mg	8.85±1.04	7.93±0.45	0.085
Total amount of propofol/mg	90.77±7.77	96.80±5.32	0.581
Aortic cross-clamp time/min	91.69±4.88	98.02±5.25	0.519

Table 3: Intra operative factors (scale variables).

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Post-operative

In Table 4, 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 3). 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) 0.00±0.000 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±.

Variable	Categories	Number of Patients				P-value
		N=13 Control (Non-delirium)		N=41 Cases (Delirium)		
		Counts	%	Counts	%	
Reoperation	No	13	100.00%	37	92.50%	0.745
	Yes	0	0.00%	3	7.50%	
The Total Time on Mechanical Ventilation/hr	0	1	0.00%	0	0.00%	0.174
	<12h	11	92.30%	40	97.60%	
	(12-24) h	1	7.70%	0	0.00%	
	(25-48) h	0	0.00%	0	0.00%	
	(49-72) h	0	0.00%	0	0.00%	
	<3days	0	0.00%	1	2.40%	
Atrial Fibrillation	No	12	92.30%	40	97.60%	0.975
	Yes	1	7.70%	1	2.40%	
Blood Transfusion	No	9	69.20%	21	51.20%	0.413
	Yes	4	30.80%	20	48.80%	
Platelet Transfusion	No	12	92.30%	36	87.80%	1
	Yes	1	7.70%	5	12.20%	

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Cardiogenic Shock	No	13	100.00%	40	97.60%	1
	Yes	0	0.00%	1	2.40%	
Post-operative Infection	No	13	100.00%	39	97.50%	1
	Yes	0	0.00%	1	2.50%	
Na> 140, neq	No	9	69.20%	30	73.20%	1
	Yes	4	30.80%	11	26.80%	
Prolonged Hypotension	No	12	92.30%	36	87.80%	1
	Yes	1	7.70%	5	12.20%	
Sleep Deprivation	No	9	69.20%	17	43.60%	0.2
	Yes	4	30.80%	22	56.40%	
Fresh Frozen Plazma-Day1	No	12	100.00%	35	85.40%	0.374
	Yes	0	0.00%	6	14.60%	
Intra-aortic Balloon Pumb-Day1	No	13	100.00%	38	95.00%	1
	Yes	0	0.00%	2	5.00%	
Bilirubin > 2 mg /dl	No	13	100.00%	39	95.10%	1
	Yes	0	0.00%	2	4.90%	
Use of Atropine	No	10	76.90%	40	97.60%	0.062
	Yes	3	23.10%	1	2.40%	
Post-operative Tachycardia	No	6	46.20%	23	56.10%	0.531
	Yes	7	53.80%	18	43.90%	
Hematocrit<30	No	7	53.80%	15	36.60%	0.27
	Yes	6	46.20%	26	63.40%	
Post-operative Pain VAS >=4	No	7	53.80%	17	41.50%	0.434
	Yes	6	46.20%	24	58.50%	
Creatinine>3mg/dl	No	11	84.60%	37	90.20%	0.955
	Yes	2	15.40%	4	9.80%	
Temperature	Normal	13	100.00%	22	53.70%	0.01
	low grade fever	0	0.00%	18	43.90%	
	high	0	0.00%	1	2.40%	
ISC Stay Days	5-Jan	9	81.80%	31	88.60%	0.338
	<10	0	0.00%	2	5.70%	
	>10	2	18.20%	2	5.70%	
Post-operative Chest Drain	<500 ml	12	100.00%	36	90.00%	0.522
	(500-	0	0.00%	3	7.50%	

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Volume	1000) ml					
	>1000	0	0.00%	1	2.50%	
Non-invasive Ventilation Use	No	7	53.80%	29	70.70%	0.26
	Yes	6	46.20%	12	29.30%	
Inotrope Post-operatively	No	6	46.20%	22	53.70%	0.637
	Yes	7	53.80%	19	46.30%	
Pao2 <70	No	11	84.60%	36	87.80%	1.00*
	Yes	2	15.40%	5	12.20%	

Table 4: Post-operative factors (categorical variables).

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 Post-operative delirium. Low and high grade fever, Post-operative morphine usage and augmenting of SOFA score are precipitating factors for Post-operative 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.

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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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