An-Najah National University

Faculty of Graduate Studies

Clinical Comparison Between Isoflurane and Sevoflurane In Patients with Open-Heart Surgery: A Prospective, Observational Study from Palestine

By

Mohammad Masoud Jaber

Superviser

Dr. Sa’ed Zyoud

Co- Supervisor

Dr. Naji Nazzal

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This Thesis was Defended Successfully on 5/ 4/ 2018 and approved by:

Defense Committee Members		Signature
1. Dr. Sa'ed Zyoud	/ Supervisor	...…………
2. Dr. Naji Nazzal	/ Co- Supervisor	…………………
3. Dr. Naser Al Hanbali	/ External Examiner	…..………
4. Dr. Aidah Alkaissi	/ Internal Examiner	…...………

Dedication

To my lovely parents

To my sisters and brothers

To my all friends

To all whom I love

Acknowledgement

وَمَا تَوْفِيقِي إِلَّا بِاللَّهِ عَلَيْهِ تَوَكَّلْتُ وَإِلَيْهِ أُنِيبُ   هود -(88)

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الإقرار

أنا الموقع ادناه، مقدم الرسالة التي تحمل العنوان:

Clinical Comparison between Isoflurane and Sevoflurane In Patients with Open-Heart Surgery: A Prospective, Observational Study from Palestine

أقر بأن ما اشتملت علية هذه الرسالة انما هو نتاج جهدي الخاص، باستثناء ما تمت الإشارة اليه حيثما ورد، وأن هذه الرسالة كاملة، أو أي جزء منها لم يقدم من قبل لنيل أي درجة أو لقب علمي أو بحثي لدى أي مؤسسة 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: **إسم الطالب:**

Signature: **التوقيع**

Date: **التاريخ:**

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Abbreviations

Abbreviation	Meaning
CABG	Coronary Artery Bypass Grafting
CHD	Coronary Heart Disease
BP	Blood Pressure
CO	Cardiac Output
CPB	Cardiopulmonary Bypass
ICU	Intensive Care Unit
HR	Heart Rate
CI	Cardiac Index
TIVA	Total Intravenous Anesthesia
SVR	Systemic Vascular Resistance
MAP	Mean Arterial Pressure
MAC	Minimum Alveolar Concentration
IQR	Interquartile Range
EF	Ejection Fraction
SBP	Systolic Blood Pressure
RR	Respiratory Rate
PONV	Post-Operation Nausea and Vomiting
CVA	Cerebral Vascular Attack
VF	Ventricular Fibrillation
LOS	Length of Stay
CCU	Cardiac Care Unit
CVP	Central Venues Pressure
ECG	Electro Cardio Gram

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Abstract

Background: volatile anesthetic agents sevoflurane and isoflurane gases can effects on hemodynamic intra- and post-operative course on-pump coronary artery bypass surgery in patients. Anesthesia type affects adequate depth of anesthesia, reduction in need of analgesic dosage, early extubation and transfer from the Intensive Care Unit (ICU).

Objectives: Study objectives were to compare the induction and recovery criteria following anesthesia with sevoflurane and isoflurane in open heart surgery, intra and post operation.

Methods: This study was an observational, cohort prospective study, it was performed at the Arab Specialized Hospital in Nablus, Heart Center in the West Bank/Palestine between May – August 2016 on all patients who were between 30-70 years and admitted to open heart surgery. All information was collected from files and observational and data collection.

The statistical package of social science (SPSS) was used for data entry in statistical analysis.

Results: During the study period, 63 patients were included, among them, 32 patients were given isoflurane, and 31 patients were given sevoflurane during open heart surgery. Systolic blood pressure (SBP) value was significantly lower in the isoflurane group compared to the sevoflurane group at the time of induction, once the sternum was opened, and once the sternum was closed ($P < 0.05$). Furthermore, diastolic blood pressure values were significantly lower in the isoflurane group compared to the sevoflurane group at the time of induction, once the sternum was opened ($P = 0.004$), and once the sternum was closed ($P = 0.009$). The median heart rate (HR) between the two groups revealed higher values in the isoflurane group, which were statistically significant when compared to the sevoflurane group at time of induction ($P < 0.001$), once the sternum was open ($P = 0.001$), and once the sternum was closed ($P = 0.010$). However, the HR values between the two groups did not reveal a statistically significant difference before induction, after Cardiac Care Unit (CCU) admission, and at extubation time ($P > 0.05$). The median respiratory rate in the isoflurane group was statistically significantly higher when compared to the sevoflurane group at extubation time ($P < 0.001$).Patients in the isoflurane group had a higher total intubation time compared to patients in the sevoflurane group ($P = 0.009$). In addition, the median (interquartile range) of the recovery time among patients in the sevoflurane group was significantly shorter than that among patients in the isoflurane group (120 (90-150) min versus 150 (120-180) min, respectively (P-value< 0.001)). Furthermore, regarding the duration of hospital stay, patients who received isoflurane had significantly longer hospital stays (7 [7-8] days) than patients who received sevoflurane (7 [6-7] days), (P = 0.012). Patients in the sevoflurane group were extubated earlier than those in the isoflurane group. Regarding complications that occurred post open heart surgery in patients, there was no significant difference regarding the prevalence of arrhythmias through or post open heart surgery among the two groups. Atrial fibrillation (AF) was seen in the isoflurane group in five (7.9%) patients, and in two patients (3.2%) in sevoflurane group (P = 0.226). Furthermore, no significant differences were noted in the type and incidence of complications regarding bleeding or cerebral vascular attack (CVA). Bleeding post open heart surgery was seen in five (7.9%) patients who were on isoflurane, and in three patients (4.8%) who were receiving sevoflurane (P = 0.372). CVA was reported in two patients (3.2%) in the isoflurane group and in none of the patients in the sevoflurane group (P = 0.254). On the other hand, nausea and vomiting occurred in nine (14.3%) patients who were administered isoflurane, but in only two (3.2%) patients who were administered sevoflurane (P = 0.026).

Conclusions: The results reflect that sevoflurane has a better impact on hemodynamic stability than isoflurane. Sevoflurane produces better results in regards to systolic and diastolic pressure, HR, recovery time, ICU stay, analgesia dosage and muscle relaxant dosage. Sevoflurane usage results in less complications than isoflurane, but not significantly.

Chapter One
Introduction

1.1. Introduction

In the 21st century, anesthesia practice is increasingly outcomes-oriented and evidence-based, yet important gaps still remain in our knowledge, even for routine clinical situations. isoflurane and sevoflurane are the most popular inhalation anesthetics in medicine today [1].

The heart includes the right atria, left atria, right ventricle and left ventricle. The atria function as inlets to receive blood, and the ventricles as outlets to eject blood from the heart [2]. The blood leaves the right ventricle to the lungs through the pulmonary artery. After oxygenation, the blood enters the left atria of the heart through the pulmonary vein. From there, the blood enters the left ventricle and is ejected into a systemic loop. Artilleries (small arteries) carry the blood through the systemic loop, starting in the aorta [2, 3]. The artilleries carry the oxygenated blood to the capillaries and deposit oxygen and collect carbon dioxide. The capillaries then transport the blood to the major veins through venues' (smaller veins). Vena cava veins lead back to heart, returning the deoxygenated blood to the heart through the right atria. When the blood moves from the right atria to the right ventricle, the cycle is repeated [2].

Open heart surgery refers to any surgery where the chest is opened and surgery is facilitated on the heart muscle, arteries, valves, or other parts of the heart, such as the aorta. "Open" refers to the fact that the chest is "cut" open [4].

The most common heart surgery done on adults is the coronary artery bypass grafting (CABG). This surgery grafts a healthy artery or vein to a blocked coronary artery. Fresh blood can then enter the heart through the grafted artery, and “bypass” the blocked one [4].

Commonly, various heart surgeries are performed in order to avoid more damage to the heart or to repair it. Open-heart surgeries are when a five to eight inch surgical cut is made into the chest wall. Besides a full open heart surgery, there is endoscopic surgery, when a surgeon will make small incisions and then complete the surgery by camera and specific endoscopic tools [5].

CABG can be required for patients with coronary heart disease (CHD); this may be facilitated through open heart surgery. When blood vessels that provide blood and oxygen for the heart become narrow and hard, CHD develops. This is regularly called “hardening of the arteries." Heart surgery is also used to replace a damaged heart with a donated heart (heart transplantation), repair damaged or abnormal areas of the heart, put in medical devices that help the heart to beat properly, and repair or replace heart valves, which allow blood to travel through the heart. Artery hardening happens when fatty material forms a plaque on the walls of the coronary arteries. This plaque narrows the arteries, which decreases the likelihood of the blood getting through. Heart attacks can happen when blood cannot flow to the heart adequately [6].

Anesthetic agents, facilitated via vaporizer, on the bypass circuit provide reduction in systemic vascular resistance (SVR) and blood pressure (BP). The BP decrease related with all the currently used volatile anesthetics is a result of vasodilatation and depression of myocardial contractility [7].

Isoflurane (2-chloro-2- (difluoromethoxy)-1, trifluoroethane) is considered a volatile, halogenated anesthetic used for inhalational anesthesia. It is a clear, stable liquid without any chemical stabilizers or additives [8]. It is the most widely used volatile anesthetic in many countries [9]. It is always rendered alongside air and/or pure oxygen, it is regularly administered with oxide, but can be induced faster with halothane (its odor can disturb the respiratory system) [10].

Isoflurane is often used to maintain a general state of anesthesia that has been initiated by another drug, such as thiopentone or propofol. It is entirely nonflammable and vaporizes readily, but is a liquid at room temperature. [11].

Sevoflurane is a halogenated anesthetic, volatile liquid for inhalation, administered by vaporization; it is a clear, stable liquid, and colorless[7]. It causes a decrease in arterial blood pressure which can be a consequence of myocardial contractility depression and decreased peripheral vascular resistance [12]. Some studies revealed that sevoflurane can provide an improved HR profile and secure cardiovascular conditions [13].

The blood-gas partition coefficient is a measure of the solubility of the inhalation anesthetic in the blood relative to its solubility in the inspired air. Circulating blood provides the means of anesthetic delivery to the brain and the partial pressure determines the rate of transfer into the CNS. The agent solubility determines how quickly the partial pressure increases in the blood [14].

Agents with high solubility (large blood-gas partition coefficients) demand that greater portions of the anesthetic dissolve in the blood before the partial pressure in the blood can increase to a level that can adequately deliver them to the brain. Therefore, agents with lower blood solubility (small blood-gas partition coefficients) have faster rates of onset of anesthesia. Desirable properties for inhalation anesthetic agents include high potency and low blood solubility [14].

Inhaled anesthetic potency is the minimum alveolar concentration (MAC) of an anesthetic agent at one atmosphere that abolishes movement in response to a noxious stimulus in 50% of subjects. MAC values for isoflurane and sevoflurane are 1.15%, 1.85% respectively, at the same atmosphere, which indicates that they both are potent and can be administered with a high concentration of oxygen [15]. Solubility of an anesthetic agent in blood is quantified as the blood to gas partition coefficient, which is the ratio of the concentration of an anesthetic in the blood phase to the concentration of the anesthetic in the gas phase, when the anesthetic is in equilibrium between the two phases. Differences in the inhaled anesthetic agents solubility in blood and tissues have significant consequences for patient recuperation from anesthesia [15]. Sevoflurane anesthesia recovery time is faster than recovery after isoflurane anesthesia [15].

Fentanyl citrate is a narcotic analgesic drug that can be used in open heart surgery to decrease and pain killer. It is used as a premedicant in low doses, and can provide analgesia during short surgical procedures. For patients requiring assisted ventilation, it is administered in higher doses and is used as an analgesic/respiratory depressant. Alongside a narcoleptic drug, fentanyl is used as part of the technique of neuroleptanalgesia. Fentanyl is also administered for severe pain, such as that of myocardial infarction [16].

In order to preserve spontaneous ventilation, lower infusion rates, e.g. 0.05 - 0.08 microgram/kg/minute, are necessary. Higher infusion rates, up to 3 micrograms/kg/minute have been used in cardiac surgery. Factors essential to estimating necessary dosage include the effect of premedicant drugs, the likely degree of surgical stimulation, and the procedure time [16].

Within the non-depolarizing blocking agents group, vecuronium bromide (Norcuron) is a muscle relaxant. Vecuronium functions by contending for the cholinoceptors at the motor end plate, which results in an exertion of its muscle-relaxing properties which are used together with general anesthesia [17]. Under balanced anesthesia, the time to recovery, to 25% of control (clinical duration), is about 25 to 40 minutes after injection;

and recovery is often 95% complete about 45 to 65 minutes after injection of intubation dose [17].

Potent inhalation anesthetics augments the neuromuscular blocking action of vecuronium. Vecuronium bromide is seen as complimentary to general anesthesia, used to aid in endotracheal intubation and to provide skeletal muscle relaxation throughout surgery or mechanical ventilation. While vecuronium bromide is usually considered as a muscle relaxant, it may be better to categorize it as a paralyzing agent. It is commercially accessible as ampoules with 4 or 10 mg of the drug in powder form, which must be dissolved in distilled water before patient administration [18].

Hemodynamic monitoring is the observation of hemodynamic parameters over time, such as blood pressure (BP), a main vital sign. BP is the pressure exerted by circulating blood upon the walls of blood vessels. "Blood pressure," when used without additional designation, often refers to the arterial pressure of the systemic circulation, which is often measured in the upper arm. Blood pressure is often shown as the systolic (maximum) pressure over diastolic (minimum) pressure and is quantified in millimeters of mercury (mm Hg) [19].

Blood pressure is determined by the endocrine and nervous systems; and changes according to activity, circumstance, and disease states. Hypotension refers to blood pressure that is pathologically low, while hypertension is pressure that is pathologically high. Both cases have many origins and can be on a spectrum from mild to severe, with acute and chronic forms. Risk of heart attack, stroke and kidney failure can be caused by chronic hypertension. In Western countries, chronic hypotension is less common than chronic hypertension. Due to a lack of clear symptoms and irregular monitorying, chronic hypertension often goes unnoticed [19].

Heart rate, or heart pulse, is the speed of the heartbeat determined by the number of poundings of the heart per unit of time, usually beats per minute (bpm). HR can differ depending on the body's physical needs, such as the need to expel carbon dioxide or consume oxygen HR changes can be caused by sleep, tension, exercise, anxiety, illness, drugs and ingestion [20].

Cardiac output (CO) is the volume of blood being pumped by the heart in one minute’s duration by a left or right ventricle. CO is calculated in various ways, for example dm3/min (1 dm3 equals 1 liter). Combined cardiac output (CCO) is the total yield from the right ventricle and the left ventricle throughout the heart’s systole phase. Common non-active CO (Q) for a human male is 5.6 L/min, and 4.9 L/min for a female [21]. The ‘time of awakening’ is defined as eye opening on verbal commands [22].

The cardiopulmonary bypass (CPB) is intended to function as the human heart and lungs to redirect blood from the patient, creating ideal surgical scenarios, oxygenate and expel carbon dioxide from the blood, chill and heat the patient’s blood and body where needed, and return blood to the patient [7]. Venous blood is drained into the venous reservoir from the right side of the patient’s heart; this reservoir is a large vessel that fuctions as the “mixing chamber” for blood, fluids, and drugs that are added to the circuit. Blood is removed from the patient primarily due to gravity or a siphon effect. Efficiency of drainage is determined by the variance in central venous pressure, height from patient on the operation room table to the venous reservoir (which is typically quite low to the ground), and any resistance in the venous circuit. From the reservoir, the blood moves immediately to the oxygenator and heat exchanger, there, oxygenation, expulsion of carbon dioxide, and cooling and warming of the blood happens. Before returning the blood to the patient through the arterial side of the circuit, it is passed through the arterial filter [7]. In-line filters eliminate any debris or air and other vents decompress the left ventricle. Cannula in the aortic root and coronary sinus supply cardioplegia solution to stop the heart throughout surgery. Safety apparatus’ in the CPB circuit includes bubble detectors, pressure monitors, and oxygen fail safe monitors. However, qualified expert perfusionists who regulate the bypass circuit, and anesthesiologists, experienced and qualified in the handling of patients sustaining cardiac surgery, cannot be replaced [7].

Cooling methods allow surgeons to arrest the heart for lengthy durations while avoiding harming the heart tissue. Cool temperatures avoid harming the heart tissue by decreasing the heart's demand for oxygen [23]. There are two ways to cool the heart, first, through a heart-lung machine. The cooled blood then decreases body temperature as it passes all body parts. The second way is through cold salt-water (saline) discharged over the heart. After cooling, the heart rate decreases and stops. To quicken the process and completely stop the heart, special potassium solution can be injected into the heart. The heart is then protected from tissue injury for two to four hours [23].

Fast tracking the cardiac surgery includes early extubation following cardiac surgery. This also results in less usage of shorter-acting neuromuscular blocking drugs or opioids, and reduced ICU or hospital lengths of stay after CABG [24].

Fast-track cardiac care is complicated; it includes many care components throughout cardiac anesthesia and in the postoperative period. The goal is post-surgery early extubation, decreasing ICU/hospital length of stay (LOS). Efficient and safe fast-track cardiac care can decrease hospital expenses [25]. Patients must be protected from infection post open heart surgery. Ochondral infections increase chances of morbidity and mortality. Most infections are commonly connected to various predisposing elements: extended perfusion duration, extra postoperative bleeding, postoperative depressed CO, and previous re-explorations for the control of hemorrhage. A vital element was the usage of bilateral internal mammary artery implants. The forcast for Sterna wound infections seems to be connected to the initial therapy adequacy and the institution of treatment duration. Staphylococcus causes a majority of these infections, but more complicated infections are usually due to fungus [26].

1.2. Problem Statement

Anesthesia practice in the 21st century is often results focused and evidence-based, yet major holes are found in our knowledge, even for prevalent clinical situations. Isoflurane and sevoflurane are now the two most popular anesthesia maintenance drugs in cardiac surgery. Most cardiac anesthesiologists believe that sevoflurane is a better cardiac anesthetic than isoflurane, yet extremely limited data is found to reinforce this idea.

Hemodynamic stability maintenance is very important in open heart surgery. These are generally very complex operations, performed in patients with associated cardiovascular disease, in whom hemodynamic instability can often cause more complications and increase risk of ischemia and further arrhythmia through induction and post open heart surgery.

Short recovery time post open heart surgery and early extubation has been found to result in decreased ICU stays, generally shorter hospital LOS and decrease nosocomial infection post open heart surgery.

1.3. The Aim of this Study

To compare the induction and recovery criteria following sevoflurane and isoflurane anesthesia in open heart surgery, intra and post operation:

1. Complications through and post open heart surgery between both gases.

2. Operation related clinical characteristics from pump time, and cardio pulmonary pump of operation.

3. Comparison between tow gases in Hemodynamic parameters pre, through and post operation.

4. Medications used among the study patients in both gases and amount of analgesia and sedation.

1.4 Significance and clinical outcome of the study

1. The results of this study will be of primary interest for open heart surgery patients and to hospitals providing postoperative pain management.

2. This study will prove to be valuable in determining induction and recovery criteria following sevoflurane and isoflurane anesthesia in open heart surgery, intra and post operation. This could aid hospital management in determining which of these agents will decrease opioid requirements.

3. The results of the study may guide anesthetists to change currently accepted anesthesia practices for patients presenting for open heart surgery.

4. The study results may guide anesthetists performing open heart surgery to change protocols with regard to analgesia given to these patients.

5. The results may provide an estimate as to whether additional analgesia should be provided pre-, intra-, and post-procedure for open heart surgery patients above the normally prescribed analgesia.

6. This study shall also be of interest to the anesthetists, and the hospital management, which as a body proposes protocols/guidelines for the safe practice of anaesthesia and pain or complications management.

Chapter Two

Literature Review

2.1. Literature Review

There are many drugs used in anesthesia, they have different functions, some of them also have many side effects. Among these broad volatile anesthetics used are; isoflurane and sevoflurane.

Volatile anesthetics reduce ischemia induced cell damage, infarct development, and infarct size by stimulating adenosine receptors, activating protein kinase C and increasing formation of nitric oxide and free oxygen radicals. Many anesthesia specialists try to use the best anesthetics in a fast track approach that assists patients to recover faster, shorten hospital LOS with less resource consumption, and decrease expenses without contributing to morbidity and mortality [13].

2.2. Isoflurane

Isoflurane is free of additives and chemical stabilizers; it is a clear, colorless, stable liquid. It can help in preserving myocardial ATP, which is important during ischemia [9]. However, it may be associated with tachycardia, which can increase the myocardial oxygen needs and can be detrimental to ischemic patients facing cardiac surgery [27], but those side effects do not appear when using sevoflurane [12]. Isoflurane is unyeilding to degradation by the absorber and can therefore be utilized during low flow or closed system anesthesia. It creates a dose-dependent decrease in blood pressure because of peripheral vasodilatation. Also, it does not sharpen the myocardium for arrhythmias. Furthermore, it can create coronary artery vasodilatation which can cause coronary artery steal syndrome [28].

During such an event blood is re-directed away from critically perfuse areas because of vasodilatation in healthy areas of the heart. This can cause myocardial ischemia or infarction. Yet, isoflurane has yet to be found as the cause for higher incidents of myocardial ischemia in clinical studies. Patients with aortic valve stenosis ought to avoid isoflurane because they are less tolerant of a decrease in systemic vascular resistance. Similar to halothane, it can cause malignant hyperthermia [28].

In regards to safety, isoflurane is known to be safe because of its low biodegradation, metabolism and stability, when exposed to CO2 absorbent [29].

2.3. Sevoflurane

Sevoflurane's odor is limited, not disturbing to the airways, and has a low blood-gas solubility coefficient [30]. In a study conducted by Ebert et al, the results showed that sevoflurane provided stable cardiovascular conditions and a better HR among their study patients [13], whereas Venkatesh et al's study showed that isoflurane and sevoflurane have similar intraoperative hemodynamic effects. Compared to isoflurane, sevoflurane had a habit of having lower HR and CI [31]. Whereas, in Lewis, et al's study, the single-breath induction with both sevoflurane and isoflurane created a major HR increase. Sevoflurane has also been shown to have improved ischemic preconditioning effects compared to other volatile agents [32].

Furthermore, some studies revealed that sevoflurane had a tendency to decrease cardiac index and HR. Eye opening and extubation were marginally sooner. Fast-tracking's primary factor is early extubation [33]. The Venkatesh et al [31] study showed that the sevoflurane group's time to awakening and extubation were quicker than in the isoflurane group, this is may be related to the requirement of fentanyl during the intraoperative period. Furthermore, in the absence of Nitrogen Oxide (N2O), patients using sevoflurane awoke much quicker compared to those using isoflurane [34]. Also, lower inotropic support was needed when using Sevoflurane. Compared with isoflurane, sevoflurane had a tendency to decrease cardiac index (CI) and HR [4].

According to Jones et al, sevoflurane was non-inferior to isoflurane in the clinically critical composite primary result of prolonged ICU LOS or 30-day mortality; in which sevoflurane had somewhat improved results compared to isoflurane [1].

Frink et al, investigated the clinical effects between sevoflurane and isoflurane in patients with good health. Sevoflurane patients recovered more quickly than those who received isoflurane. They also felt less confusion and better coordinated than those who received isoflurane, but sevoflurane patients also had increased pain scores [35].

In the Venkatesh et al, study, neither group showed a major rise in cardiac enzymes in the postoperative period. Sevoflurane and isoflurane can harmlessly be utilized for fast track anesthesia. However, sevoflurane causes earlier awakening and extubation than isoflurane [31]. Sevoflurane induction was easier and faced less obstacles than isoflurane induction [35].

Regarding the costs, for a 4.5 hour, normal, cardiac surgical procedure, the price per patient for isoflurane was $4.24, whereas sevoflurane was $58.92[36]. In comparison to propofol, sevoflurane patients had decreased myocardial injury in the first 24 postoperative hours[37]. Also, postoperative Troponin-I concentrations and demand for prolonged inotropic support were less in patients receiving sevoflurane [21].

One study saw comparable pharmacokinetics in wash-in and wash-out for sevoflurane and isoflurane. Also, cardiovascular stability differences were not seen. The cardiac damage markers were the same for the two anesthetics. This data shows that sevoflurane and isoflurane can similarly be used in patients undergoing CABG surgery with extracorporeal circulation [38].

2.4. Clinical Implications

A study conducted by Özgök et al [39] aimed to compare the myocardial protective effects of fentanyl-based total intravenous anesthesia (TIVA), sevoflurane and isoflurane. This double-blinded, randomized study categorized the samples into three groups. The first group, TIVA, the second, sevoflurane, and the third, isoflurane. In the second and third groups, maintenance doses of fentanyl 5 µg/kg and pancuronium bromide 2 mg were administered regularly. However, in the first group, the control group, the fentanyl (0.25-0.5 µg/kg/min) and midazolam (0.3 mg/kg/min) were administered by intravenous infusion, and pancuronium was rendered in a prescription of 2 mg, as mandatory.

The study showed that compared to the patients in the TIVA group, at the T3 period before CPB, there was a compelling decrease in the sevoflurane and isoflurane group in the SVR amounts. At the T3 period, the CI and CO values did not differ between the groups; however, all group values greatly increased over the T3 values, without a major differences between the groups, at the T4 period (after CPB measurement) [39].

In a study by Malan et al [40], it was shown that, compared to awake values, sevoflurane did not change HR. Sevoflurane lowered stroke volume index, MAP, and mean pulmonary artery pressure at all anesthetic concentrations. CI reduced compared to awake measurements at 1.0 and 1.5 MAC, but not at 2.0 MAC, where SVR reduced. Central venous pressure declined somewhat, compared to awake values at 1.5 MAC, but not at 1.0 or 2.0 MAC. Mixed venous hemoglobin saturation intensified at all anesthetic concentrations, but complete body oxygen usage lowered at all anesthetic concentrations. Arterial base-excess was unaltered. Sevoflurane did not change the velocity of circumferential fiber shortening or the left ventricular area ejection fraction. Systolic wall stress was reduced at all anesthetic concentrations. Left ventricular end-diastolic area was unaltered, as prescribed by the experimental customs [40].

Isoflurane increased HR to 1.5 and 2.0 MAC. Compared to awake measurements at 1.0 MAC, CI reduced but not at 1.5 and 2.0 MAC where SVR decreased. Systolic wall stress, mean arterial pressure (MAP), and stroke volume index reduced at all anesthetic concentrations. Mixed venous hemoglobin saturation was higher at all isoflurane concentrations, but complete body oxygen consumption decreased at 1.5 and 2.0 MAC. Additional measured variables were not altered [40].

In a study which set out to compare the gases, Venkatesh et al [31] found that the top-up amount of fentanyl was remarkably increased in isoflurane (265 μg± 36) than sevoflurane (150 ± 36 μg, $P < 0.001$). The fentanyl usage in the TIVA group was quite high compared to the volatile anesthetic groups (TIVA 6643.82 micgr ±1184.92; sevoflurane group 2485.00 micgr ±184.85; isoflurane group 2441.25 micgr ±174.76). Also, Ejection Fraction (EF) increased in the sevoflurane group but declined in the TIVA and isoflurane groups[31].

A study conducted by Mourad et al, concluded that sevoflurane combined with a low dose of fentanyl resulted in early extubation in a group of 75 patients undergoing CABG. Early extubation is a benefit of Off-pump Coronary artery bypass (OPCAB). This was achieved in our study. The sevoflurane group had a decreased fentanyl demand throughout the intraoperative period, this may be one of the early awakening causes for this group [41].

In a study conducted by Bennett et al [30], it was shown that both agents (sevoflurane and isoflurane) have comparable hemodynamic effects at 0.5 and 1.0 minimum alveolar concentration. Common factors included a decrease in heart rate, cardiac output and blood pressure, but filling pressures stayed constant with each volatile agent. Electrocardiography did not reveal ischemic changes. Eye opening and extubation times were alike for the two agents, with sevoflurane disposed to be sooner than isoflurane [30].

In another study, Malan et al [40] found that both agents, sevoflurane and isoflurane, displayed comparable hemodynamic effects at 0.5 and 1.0 minimum alveolar concentration. Decreases in heart rate, blood pressure, and cardiac output were common, while filling pressures continued to be secure with each volatile agent. Electrocardiography did not show ischemic changes. Eye opening and extubation times were alike with both agents, with sevoflurane often sooner than isoflurane. Compared with isoflurane, sevoflurane often decreased heart rates and CI. However, these results were not statistically significant [40].

The Chinese study by Chen et al [42] offers similar alterations in systolic and diastolic arterial pressure during maintenance in comparison between sevoflurane and isoflurane. After surgical incision, the HR accelerated more in isoflurane patients ($p < 0.05$). During emergence, time of response to command was significantly shorter in patients receiving sevoflurane than patients receiving isoflurane (5.6 +/- 0.4 min versus 15.2 +/- 3.0 min, $p < 0.001$). Side effects, like nausea and vomiting, were similar in the two groups [42].

In a randomized, prospective, controlled trial of time to tracheal extubation, post coronary artery surgery with sevoflurane, isoflurane, or target-controlled propofol anesthesia, Parker et al [43] reported that the median time to tracheal extubation for the propofol group was 10.25 hours (interquartile range [IQR] 8.08-12.75), the sevoflurane group, 9.17 hours (IQR 6.25-11.25), and the isoflurane group, 7.67 hours (IQR 6.25-9.42). Intraoperative, the propofol group demanded lower vasopressor ($p = 0.002$) and higher vasodilator therapy (nitroglycerin $p = 0.01$, nitroprusside $p = 0.002$). The groups did not differ in regards to time to ICU discharge [43].

A study conducted by Karlsen et al [44] aimed to compare desflurane, sevoflurane and isoflurane. The time to opening of eyes and impact on respiration was comparable in all three anesthetics. As the emergence from anesthesia did not change remarkably between the three agents [44].

A study conducted by Sahu et al [45] aimed to evaluate isoflurane and sevoflurane as maintenance anesthetic agents in day care surgeries in regards to intraoperative hemodynamics, negative effects, recovery profile, time of first postoperative analgesia and pain score. Two groups of 30 patients were randomly chosen to take isoflurane or sevoflurane as a maintenance agent. Both groups experienced limited nausea and no significant differences were found between both groups, Both groups had like times for the requirement of first post op analgesia ; median±IQR in Group I was 53.0±19 min and in Group S it was 54.5±15 min. Analysis by the Mann-Whitney test displayed an insignificant P value of 0.094 [45].

In a CPB study which set out to determine the sevoflurane and isoflurane pharmacokinetics, hemodynamic stability, and cardio protective effects, Freiermuth et al [33] found comparable pharmacokinetics concerning wash-in and wash-out for sevoflurane and isoflurane. Variances in cardiovascular stability were also absent. Cardiac damage markers were the same for both anesthetics. For patients undergoing coronary artery bypass graft surgery with extracorporeal circulation, sevoflurane and isoflurane may equally be used according to this data [33].

In a study investigating the hemodynamic criterion of low-flow isoflurane and low-flow sevoflurane anesthesia in controlled ventilation with a laryngeal mask airway, Chavan et al [46] reported that the mean HR values were much lower in the sevoflurane group (P value < 0.05) 25 minutes post-surgery. Isoflurane group mean blood pressure was at increased levels compared with the sevoflurane group 10, 20 and 30 minutes post-surgery (P values = 0.0131, 0.0373 and 0.0028, respectively). However, HR and mean blood pressure were in the average range, therefore, these variations were clinically insignificant [46].

A study conducted by Karlsen et al [44] aimed to compare desflurane, sevoflurane and isoflurane anesthesia in reference to recovery and postoperative nausea and vomiting post surgery. Desflurane had a significantly higher 24 hour post-operation nausea and vomiting (PONV) rate compared to isoflurane. Early PACU PONV rate was much less ($P<0.05$) for the more soluble isoflurane (4%) compared to the low soluble gases, desflurane and sevoflurane together (28%) [44].

Navarro et al, research showed that sevoflurane and isoflurane anesthetization has similar arrhythmic reaction as epinephrine. Sevoflurane and isoflurane are the same in their sensitization of the human myocardium to the arrhythmogenic effect of exogenously rendered epinephrine [47].

2.5. On-pump open heart surgery

Coronary artery surgery can be performed with or without CPB, known as the beating heart or off-pump technique. On-pump CABG is an operation that is conducted after stopping the heart. When the heart is stopped, blood supply is cut off to the rest of the body. Surgeons must then use an artificial circulation mechanism that functions like the heart and the lungs, the CPB machine (heart-lung machine or the pump) [48]. Cannulas (pipes) are positioned in the heart to drain unwanted blood to the pump, after purification it is returned to the patient. Hence, specialized medications can not only stop the heart safely but also sustain it while the bypass grafts are created [48]. Afterwards, the heart resumes its work and the CPB machine is detached after the cannulas are removed from the heart. On-pump CABG today has a small risk of death or obstacles, is a safe operation. For a low-risk patient, the average risk is 1% to 2%. Other health-threatening concerns change the amount of risk. Stroke, kidney or liver failure, decrease in higher mental function, and bleeding are some of the potential concerns. These concerns have been attributed to the usage of the pump and the necessity of manipulating both the large arteries and the heart in order to start the patient on the system. Updated technology has made the heart-lung machine very safe [48]. Surgeons have understood the complexities and have learned to be aware of them and to take vital precautions [49]. Bypass grafts created on a stopped heart are considered to be complete and superior to other approaches [11].

Chapter Three
Methods

3.1. Study Design

This study was designed as a cohort prospective study to compare isoflurane and sevoflurane intra and post open heart surgery and investigate hemodynamics and recovery time in the Arab Specialized hospital in Nablus city.

3.2. Study Setting

This study conducted in the operation room and ICU in the Arab Specialized hospital, which is located in Nablus, a large city in north Palestine from May – August 2016 This hospital is considered the largest center of open heart surgery in the north West Bank and conducts a large number of operations. The hospital is composed of eight floors, including an emergency room, medical and surgical ward, ICU, CCU, gynecology department, pediatric and neonatal ICU.

The total capacity of the hospital is 76 beds in all specialties, the Arab heart center contains five beds in CCU, and 13 beds as intermediate. Intermediate has five rooms, which admits the catheterization patients, and receives patients after their time in CCU, the CCU is fully monitored and prepared for admitting full emergency cases, and every bed side has its own ventilator, monitor and ICU equipment. The intermediate is fully monitored and every bed is ready to have an emergency case temporarily. The center admits about 150-200 patients every month, some are for open heart surgeries, others for cardiac catheterization and stenting. 20-40 open heart surgeries are performed monthly in the center.

The center has a well-qualified team composed of 22 nurses in CCU who are trained for taking care of very complex cases post open heart surgeries, six nurses who work in the operation theatre, and four nurses in the catheterization lab.

There are two cardio-thoracic surgeons, three cardiologists, an ICU specialist, and four resident doctors in the center who work 24 hours, seven days a week. Protocols and policies in the Arab Specialist hospital describe the care of patient from admission time to discharge and follow up.

3.3. Study Population

Upon receiving approval from the Hospital Ethics Committee and IRB, informed consent was obtained from sixty three patients, planning to undergo elective CABG, between 30-70 years, admitted to the Arab specialized hospital and, belonging to the American Society of Anesthesiologists, physical status II-IV and New York Heart Association class I or II.

Common cardiac medications can affect the hemodynamics of the heart, and decrease patient complications that may occur while waiting for an operation. And stop at night and effect can finished at the morning before the operation due to no effect and decreases the biased and differences in the comparison between all the patient . Protocol allows for midazolam or other drugs to decrease anxiety.

Once the patient is ready on the operation table, they are connected to monitors and the Cannula, CVP and arterial line are applied. Folic catheters to monitor urine output is also necessary in order to monitor the operation and provide vital organ perfusion. After the invasive line is applied anesthesia is begun, as well as hypnotic drugs, propofol and midazolam, followed by muscle relaxant and good ventilation. Narcotics drugs are provided to decrease pain and maintain hemodynamic stability. IV fluids and norepinephrine and epinephrine infusion (0.05 – 0.1 μg/Kg/min) were administered. Nitroglycerine infusion was available to maintain MAP if necessary (from 65-75). Hemodynamic measurements included HR, central venous pressure (CVP), CI, and MAP at baseline, post-induction after completing coronary anastomosis, and prior to moving the patient to recovery. The total quantity of volatile anesthetic agent utilized for each patient was determined using the formula (Dion) = dialed concentration (%) x total fresh gas flow (L/min) x duration at that concentration (min) x molecular weight (gms) divided by 2412 x density (g/L). Total amount of opioid analgesic used, intraoperative, was recorded for each group (isoflourane and sevoflourane) and a 32c temperature in hypothermia stage was maintained. Postoperatively, the time of awakening by means of eye opening on verbal commands and extubation in the postoperative recovery ward was completed after good movement of extremities, elevation of the head and temperature reaching to 36 c axillary can do extubation.

3.4. Inclusion criteria

The study will include patients 30-70 years old undergoing on-pump open heart surgery. This age range is chosen because patients tend to be healthy and that will limit confounders, other factors that could affect the study. Ages over 70 face higher incidences of weak muscle and can increase incidences of other factors which could affect the study.

Also, patients included belong to the American Society of Anesthesiologists, physical status II-IV and New York Heart Association class I or II, scheduled to undergo elective CABG .and good ejection fraction (EF) above 40%.

3.5 Exclusion Criteria

Patients who died in the operation room, obese patients (pt over BMI >30), severe renal or hepatic disease, redo surgery, severe cardiac dysrhythmias or a left ventricular EF below 40%. Those with respiratory complications or older than 70 years old, because these ages have higher incidence of lung complications, weak muscle, rheumatic arthritis, and valve diseases. As well as patients who have surgery completed by off-pump way.

3.6 Ethical Considerations

After receiving approval from Hospital Ethics Committee:

- Permission for the study obtained from the Arab specialized hospital director.

- Approval of the study asked from the ANU research committee (IRB).
- A consent form from the client or their family was necessary to participate in the study.
- All information provided by the clients or their health conditions is handled confidentially.

3.7 Sample Size

The study included 63 patients admitted to the Arab specialized hospital. Thirty tow patients used isoflurane and 31 patients used sevoflurane intra and post open heart surgery; hemodynamic stability and recovery time was studied for both gases.

3.8 Variable Definition

3.8.1 Dependent Variables

1. Post open heart surgery (ICU) stay and hospital (LOS).
2. Complications through and post open heart surgery between sevoflurane and isoflurane anesthesia.
3. Intraoperative time intervals, recovery time, and duration of hospital between two anesthesia groups.
4. Hemodynamic parameters among patients in isoflurane and sevoflurane groups.
5. Dose of medications used in isoflurane and sevoflurane groups.

3.8.2 Independent Variable:

1- Age of the patient.

2- Gender of the patient.

3- Smoking.

4- Rheumatoid arthritis.

5- Diabetes militias.

6- History of old surgery .

7- Hypertension.

8- Body mass index.

9- Type of inhalation gases (isoflurane and sevoflurane).

10- Amount of analgesia and narcotic dose.

11- Time duration and pump time in both gases.

3.9 Data Collection Tools

Abstraction data sheet design for data collection, including five sections:

1. Patient characteristics (age, gender, smoking, previous history, hypertension, diabetes mellitus, rheumatoid arthritis, body mass index).

2. Complications through and post open heart surgery (bleeding, arrhythmia, cerebral vascular attack, and nausea and vomiting).

3. Operation related clinical characteristics (operation time, pump time, recovery time, duration state in the hospital, and intubation time from minute measurement)

4. Hemodynamic parameters pre, intra, and post-operation including systolic blood pressure, HR, diastolic pressure, respiratory rate, and central venues pressure. Including monitoring of five-lead ECG, with thermodilution, CO measurement, pulse oximetry, capnography and blood temperature. (Phillips Medical System Pvt. Ltd, M1166A, Andover, Netherland)

5. Medications used among the study patients (fentanyle, morphine, paracetamol, and vecuronium)

3.10 Follow up period

Patient follow up was continued until extubation and length of stay in ICU and hospital.

3.11 Data Analysis

The data was analyzed using the Statistical Package for Social Sciences (SPSS Inc version 16). Descriptive statistics was performed for all variables and expressed as frequency and percentage for categorical variables and median [interquartile range] for continuous variables. Fisher's exact tests or Pearson chi-square were used to compare categorical variables, as appropriate. The Kolmogorov–Smirnov statistic was utilized in testing the normality of continuous variables. Since most of the variables did not follow a normal distribution. The Mann – Whitney U-test was used for the comparison of open heart surgery between isoflurane and sevoflurane.

Chapter Four
Results

4.1 Socio-demographic characteristics of the study sample

A sum of 63 patients participated in the research, among them, 32 patients were given isoflurane and 31 patients were given sevoflurane during open heart surgery.

The socio-demographic data of the study patients are shown in Table 4.1. There is not a notable difference between the patients receiving sevoflurane or isoflurane with respect to gender, age, body mass index, presence of hypertension, presence of rheumatoid arthritis, previous surgery, preoperative cardiac hemodynamic status, New York heart association classification, and ASA physical classification. On the other hand, 23 patients who received isoflurane had diabetes mellitus compared to 13 patients in the sevoflurane group (P = 0.016).

Table 4.1: Patient Characteristics for Isoflurane and Sevflurane Groups.

Variable	Frequency (%) or Median [interquartile range]	Isoflurane N=32 (%) or Median [interquartile range]	Sevoflurane N=31(%) or Median [interquartile range]	P value
Age (mean)	60 [56-65]	62 [59.25-65]	58 [53-65]	0.079
Gender				
Male	55 (87.3)	27 (84.4)	28 (90.3)	
Female	8 (12.7)	5 (15.6)	3 (9.7)	0.708
Smoking				
Yes	33 (52.4)	13 (40.6)	20 (64.5)	
No	30 (47.6)	19 (59.4)	11 (35.5)	0.058
BMI				
Under	14 (22.2)	8 (25.0)	6 (19.4)	
Normal	49 (77.8)	24 (75.0)	25 (80.6)	0.590
Diabetes Mellitus				
Yes	36 (57.1)	23 (71.9)	13 (41.9)	
No	27 (42.9)	9 (28.1)	18 (58.1)	0.016
Hypertension				
Yes	33 (52.4)	18 (56.3)	15 (48.4)	
No	30 (47.6)	14 (43.8)	16 (51.6)	0.532
Rheumatoid Arthritis				
Yes	1 (1.6)	0 (0.0)	1 (3.2)	
No	62 (98.4)	32 (100.0)	30 (96.8)	0.492
Previous Surgery				
Yes	26 (41.3%)	16 (50)	10 (32.3)	
No	37 (58.7%)	16 (50)	21 (67.7)	0.153

Abbreviation: ASA: American Society of Anesthesiology Classification, BMI: body mass index.

4.2 Complications Through and Post Open Heart Surgery

Table 4.2 compares the complications that occurred post open heart surgery in patients given sevoflurane and isoflurane as an anesthetic agent. There was no significant difference regarding the prevalence of arrhythmias through or post open heart surgery among the two groups. Atrial fibrillation

(AF) was seen in the isoflurane group in five (7.9%) patients, and in two patients (3.2%) in the sevoflurane group (P = 0.226). Furthermore, limited differences were noted in the type and incidence of complications regarding bleeding or CVA. Bleeding post open heart surgery was seen in five (7.9%) patients who were on isoflurane, and in three patients (4.8%) who were receiving sevoflurane (P = 0.372). Cerebral vascular attack was reported in two patients (3.2%) in the isoflurane group and in no patients in the sevoflurane group (P = 0.254). On the other hand, nausea and vomiting occurred in nine (14.3%) patients who were administered isoflurane, but in only two (3.2%) patients who were administered sevoflurane (P = 0.026).

Table 4.2: **Complications Post Open Heart Surgery Between Sevoflurane and Isoflurane Anesthesia**.

Variable	Frequency (%)	Isoflurane N=32 (%)	Sevoflurane N=31 (%)	P value [a]
Bleeding				
Yes	8 (12.7)	5 (7.9)	3 (4.8)	0.372
No	55 (87.3)	27 (42.9)	28 (44.4)	
Cerebral Vascular Attack				
Yes	2 (3.2)	2 (3.2)	0 (0)	0.254
No	61 (96.8)	30 (47.6)	31 (49.2)	
Arrhythmia				
Yes	7 (11.1)	5 (7.9)	2 (3.2)	0.226
No	56 (88.9)	27 (42.9)	29 (46)	
Nausea and Vomiting				
Yes	11 (17.5)	9 (14.3)	2 (3.2)	**0.025**
No	52 (82.5)	23 (36.5)	29 (46)	

[a] The p-values are bold where they are less than the significance level cut-off of 0.05.

4.3 Operation Related Clinical Characteristics

Operative characteristics are shown in Table 4.3. No major difference was seen regarding the total operation time, and the pump duration time in patients who were given isoflurane or sevoflurane (P > 0.05). However, patients in the isoflurane group had a higher total intubation time compared to patients in the sevoflurane group (P = 0.009). In addition, the median (interquartile range) of the recovery time among patients in the sevoflurane group was significantly shorter than that among patients in the isoflurane group (120 (90-150) min versus 150 (120-180) min, respectively (P-value< 0.001)). Furthermore, regarding the duration of hospital stay, patients who received isoflurane had a significantly longer hospital stay (7 [7-8] days) than patients who received sevoflurane (7 [6-7] days), (P = 0.012).

Patients in the sevoflurane group were extubated earlier than the isoflurane group.

Table 4.3 Intraoperative time intervals, recovery time, and duration of hospital stay between the two anesthesia groups.

Variable	**Total Median [**interquartile range**] N=63**	**Isoflurane Median [**interquartile range**] N=32**	**Sevoflurane Median [**interquartile range**] N=31**	**P value** [a]
Total operation time (minute)	210 [195-240]	210 [199-240]	210 [180-240]	0.989
Pump duration time (minute)	68 [59-90]	69 [59.25-90]	66 [56-90]	0.654
Total time of intubation (minute)	360 [330-390]	360 [330-420]	330 [310-360]	**0.009**
Recovery time (minute)	120 [105-150]	150 [120-180]	120 [90-150]	<**0.001**
Duration of hospital (day)	7 [6-8]	7 [7-8]	7 [6-7]	**0.012**

[a] The p-values are bold where they are less than the significance level cut-off of 0.05.

4.4 Hemodynamic Parameters pre, through and post operation

Table 4.4 outlines the hemodynamic parameters pre, through and post open heart surgery between the isoflurane and sevoflurane groups. SBP values were much lower in the isoflurane group compared to the sevoflurane group at the time of induction ($P = 0.035$), once the sternum was opened ($P < 0.001$), and once the sternum was closed ($P = 0.001$). Furthermore, diastolic blood pressure values were much lower in the isoflurane group compared to the sevoflurane group at the time of induction ($P = 0.026$), once the sternum was opened ($P = 0.004$), and once the sternum was closed ($P = 0.009$). However, both SBP and diastolic blood pressure values were not much different between the two groups pre-induction, after admission to CCU, and at extubation time ($P > 0.05$).

On the other hand, median HR revealed higher values in the isoflurane group which were statistically notable when compared to the sevoflurane group at time of induction ($P < 0.001$), once the sternum was open ($P = 0.001$), and once the sternum was closed ($P = 0.010$). However, the HR values between the sevoflurane and isoflurane groups did not show a statistically notable difference before induction, after CCU admission, and at extubation time ($P > 0.05$).

Regarding the patients' respiratory rate, the median of respiratory rate in the isoflurane group was statistically much higher when compared to the sevoflurane group at extubation time ($P < 0.001$). However, there were no differences in respiratory rate values between the two groups before induction, and after CCU admission (P > 0.05).

Furthermore, in comparison of central venous pressure between the two groups, there were no notable differences between the two groups at time of induction, once the sternum was opened or closed, after CCU admission, and at extubation time (P > 0.05), (Table 3.4).

Table 4.4 Hemodynamic parameters among patients in isoflurane and sevoflurane groups.

Variable	**Median [interquartile range]**	**Isoflurane Median [interquartile range] N=32**	**Sevoflurane Median [interquartile range] N=31**	**P value**
Systolic Blood Pressure				
Pre-operative	130 [120-140]	130 [130-137.25]	130 [120-140]	0.346
Induction	110 [100-110]	105 [100-110]	110 [100-115]	**0.035**
Open sternum	90 [85-100]	90 [82-90]	98 [90-100]	**<0.001**
Closed sternum	90 [82-100]	83 [80-95]	98 [90-102]	**0.001**
CCU admitted	110 [99-121]	109.5 [96-117]	112 [99-128]	0.223
Extubation time	125 [113-134]	120 [112-135]	128 [113-133]	0.720
Diastolic Blood Pressure				
Pre-operative	78 [69-80]	80 [70-80]	70 [65-80]	0.170
Induction	60 [50-66]	58 [50-65]	60 [56-70]	**0.026**
Open sternum	50 [48-60]	50 [45-50]	50 [50-60]	**0.004**
Closed sternum	50 [50-60]	50 [45-54]	55 [50-60]	**0.009**
CCU admitted	60 [52-65]	60 [48-65]	60 [55-65]	0.402
Extubation time	66 [60-76]	63 [60-76]	68 [60-78]	0.917
Heart Rate				
Pre-operative	78 [75-82]	80 [75-84]	77 [72-80]	0.066
Induction	78 [70-85]	80 [78-87]	72 [70-80]	**<0.001**
Open sternum	72 [65-78]	75 [70-79]	68 [62-74]	**0.001**
Closed sternum	72 [67-78]	74 [70-78]	69 [63-75]	**0.010**
CCU admitted	80 [74-88]	80 [73-88]	80 [74-92]	0.901
Extubation time	90 [80-98]	91 [88-99]	89 [79-98]	0.130
Respiratory Rate				
Pre-operative	19 [18-20]	19 [16-21]	19 [18-20]	0.769
CCU admitted	14 [14-15]	14 [14-15]	14 [14-15]	0.498
Extubation time	20 [19-23]	22 [20-27]	20 [16-20]	**<0.001**

CVP				
Induction	5 [4-6]	5 [4-6]	4 [4-6]	0.104
Open sternum	4 [3-6]	4 [3-6]	5 [4-6]	0.525
Closed sternum	3 [2-5]	4 [2-5]	3 [2-4]	0.329
CCU admitted	5 [3-6]	5 [3-7]	4 [3-6]	0.458
Extubation time	5 [4-8]	6 [3 -8]	5 [4-8]	0.819

Abbreviations: CCU: cardiac care unit, CVP: central venous pressure.

[a] The p-values are bold where they are less than the significance level cut-off of 0.05.

4.5 Medications used among the study patients

As shown in Table 4.5, the median dose [interquartile range] of fentanyl was 600 mic [550-737] for patients given isoflurane versus 550 mg [500-600] for patients given sevoflurane, (P = 0.004). Furthermore, the median dose [interquartile range] of morphine sulfate was much higher in the isoflurane group compared to the sevoflurane group (10 mg [5-10] versus 10 mg [10-15], (P = 0.002)). In addition, regarding the skeletal muscle used, patients on isoflurane were given a higher vecuronium dose compared to patients on sevoflurane (14 [12-14] versus 12 [12-14], (P = 0.015)). However, the median dose of paracetamol administered after surgery did not differ between the isoflurane group and the sevoflurane group (P > 0.057).

Table 4.5: Dose of medications used in isoflurane and sevoflurane groups .

Variable	**Median [**interquartile range**]**	**Isoflurane Median [**interquartile range**] N=32**	**Sevoflurane Median [**interquartile range**] N=31**	**P value [a]**
Fentanyl dose (mic)	600 [500-650]	600 [550-737]	550 [500-600]	**0.004**
Vecuronium dose	13 [12-14]	14 [12-14]	12 [12-14]	**0.015**
Paracetamol dose	1 [1-1]	1 [1-1]	1 [1-1]	0.057
Morphine dose	10 [10-10]	10 [10-15]	10 [5-10]	**0.002**

[a] The p-values are bold where they are less than the significance level cut-off of 0.05.

Chapter Five
Discussion

5.1 Hemodynamic parameters among patients in isoflurane and sevoflurane groups

Study results show that patients administered sevoflurane for on -pump coronary vascular surgery were safer through and post open heart surgery than patients administered isoflurane for the same intervention. Sevoflurane provided stable cardiovascular conditions through operation and a better HR profile in patients undergoing selective surgery compared to isoflurane volatile anesthetics.

The current study evaluated the hemodynamic parameters pre, through and post open heart surgery between the isoflurane and sevoflurane groups. SBP values were much lower in the isoflurane group compared to the sevoflurane group at the time of induction, opening the sternum, and once the sternum was closed, diastolic blood pressure values were much lower in the isoflurane group compared to the sevoflurane group at the time of induction, opening the sternum, and once the sternum was closed. However, both SBP and diastolic blood pressure values were not much different between the two groups pre-induction, after admission to CCU, and at extubation time.

These results comply with those obtained by Sahu et al [45], who suggested that intraoperative hemodynamics such as SBP, was lower in isoflurane compared to sevoflurane, and diastolic blood pressures (DBP) was stable in sevoflurane compared to isoflurane [45].

The results shown in this study are in agreement with data obtained by Ebert et al, who showed that sevoflurane provided stable cardiovascular conditions [13]. The Sohrab et al [28] findings are consistent with the results in this current study, which found the mean blood pressure in the isoflurane group was much higher compared to the sevoflurane group 10, 20 and 30 minutes post-surgery [28].

These results are also in agreement with Malan et al, findings that sevoflurane reduced MAP, mean pulmonary artery pressure, and stroke volume compared to isoflurane [40].

The results shown in this study are not agreement with data obtained In a Chinese study which compared sevoflurane and isoflurane in hemodynamics and recovery of anesthesia in Chinese adult patients, sevoflurane and isoflurane caused similar alterations in systolic and diastolic arterial pressure during maintenance [42]. Venkatesh et al, is an another study which has shown that isoflurane and sevoflurane have similar intraoperative hemodynamic effects [31].

The outcome of this study is contrary to that of Freiermuth et al, which saw comparable pharmacokinetics regarding wash-in and wash-out for sevoflurane and isoflurane. Furthermore, no change in cardiovascular stability was seen [38].

This study found that the median HR between the two groups revealed higher numbers in the isoflurane group which were statistically notable in comparison to the sevoflurane group at time of induction, opening the sternum, and once the sternum was closed. However, the HR values between the two groups did not show a statistically remarkable difference before induction, after CCU admission, and at extubation time. Regarding the patients' respiratory rate, the median of RR in the isoflurane group was statistically quite higher when compared to the sevoflurane group at extubation time. However, there were no differences in respiratory rate values between the two groups before induction, and after CCU admission.

These results further support the idea of Sahu et al [45] , which found that HR and PR were comparable in both sevoflurane and isoflurane groups. This study also matches the findings of Ebert et al [34] which showed that sevoflurane provided stable cardiovascular conditions and a better HR among their study patients compared to patients who received isoflurane anesthesia [34]. Our study results are in line with those of a previous study conducted by Bennett et al [30], in patients undergoing valvular cardiac surgery, which found that compared with isoflurane, sevoflurane displayed a tendency to decrease heart rates.

5.2 Intraoperative time intervals, recovery time, and duration of hospital stay between the two anesthesia groups.

An important factor to the study was Fast Track; the fast track method allows patients to recuperate faster and shorten the hospital stay and critical care period while decreasing expenses, and resource use but still not impacting mortality and morbidity. Improved surgical techniques, utilizing ultra short acting drugs, less narcotics usage, and adhering to early weaning protocols makes this option possible. Early extubation is the most prominent element of fast-tracking, which is within 1-6 hours of surgery. This is dependent on the utilized surgical techniques and anesthetic.

The current study found that no major difference was seen regarding the total operation duration, and the pump duration time in patients who were given isoflurane or sevoflurane ($P > 0.05$). However, patients in the isoflurane group had a higher total intubation time compared to patients in the sevoflurane group. In addition, the median (interquartile range) of the recovery time among patients in the sevoflurane group was much lower than that among patients in the isoflurane group (120 (90-150) min versus 150 (120-180) min, respectively. Furthermore, regarding the duration of hospital stay, patients who received isoflurane had significantly longer hospital stays (7 [7-8] days) than patients who received sevoflurane (7 [6-7] days).

The most obvious finding to emerge from the analysis is that patients in the sevoflurane group were extubated earlier than the isoflurane group. This data matches that of Venkatesh et al, sevoflurane data showed extubation and eye opening somewhat sooner. Early extubation is the primary component of fast-tracking [31].

In a study conducted by Elbert et al [34], it was shown that the awakening and extubation time was less in the sevoflurane group compared to the isoflurane group [34].

These results further support the idea in a Chinese study by Chen et al [42] which compared hemodynamics and recuperation using sevoflurane and isoflurane anesthesia on Chinese adult patients. It showed that the time of response to command was much less in patients receiving sevoflurane than patients receiving isoflurane (5.6 +/- 0.4 min versus 15.2 +/- 3.0 min [42]. The results of our study are consistent with data obtained by Frink et al, the study showed that sevoflurane patients experienced less confusion and were more coordinated than those who had been administered isoflurane. Higher pain scores were also found in sevoflurane patients. Sevoflurane induction had less complications and tended to be smoother compared to isoflurane induction [35].

These results further support the idea in a study conducted by Mourad et al, which saw early extubation when sevoflurane was administered with a low dose of fentanyl [41].

Which finding do not reflect those obtained by Jones et al, who found that, in the clinically valuable composite primary outcome of prolonged ICU LOS, sevoflurane was non-inferior to isoflurane [22]. Furthermore, this outcome is contrary to that of Ayşegül Özgök et al [50] (2001), who found that the mechanical ventilation periods (MVP) were alike in the TIVA, Sevoflurane, and Isoflurane groups postoperatively (8.04±0.2 hours;

7.8±0.1 hours; 8.02±0.2 hours, respectively). ICU stays were also alike in all the groups (14.4±0.2 hours; 13.9±0.3 hours; 14.1±0.3 hours, respectively) as well as hospital stays (HS) (4.9±0.1 days; 5.2±0.1 days; 5.4±0.3 days, respectively).

This study has been unable to demonstrate what Parker et al did, that time to tracheal extubation after coronary artery surgery with isoflurane was less than sevoflurane. ICU discharge times were the same for all groups [43]. The outcome of this study is contrary to that of Karlsen et al, who researched the time of extubation anesthesia recovery and postoperative nausea and vomiting after breast surgery. Desflurane, sevoflurane and isoflurane anesthesia's time to eye opening and influence on respiration was alike. The emergence from anesthesia did not change much between the three anesthesia [44].

5.3 Dose of medications used in isoflurane and sevoflurane groups.

An important, clinically relevant finding was that patients in the sevoflurane group required a significantly lower dose of analgesia than the isoflurane group.

The current study found the median dose [interquartile range] of fentanyl was 600 mic [550-737] for patients given isoflurane versus 550 mg [500-600] for patients given sevoflurane, (P = 0.004). Furthermore, the median dose [interquartile range] of morphine sulfate was much higher in the isoflurane group compared to the sevoflurane group (10 mg [5-10] versus 10 mg [10-15], (P = 0.002)). In addition, regarding the skeletal muscle used, patients using isoflurane were given a higher vecuronium dose compared to patients using sevoflurane (14 [12-14] versus 12 [12-14], (P = 0.015)). However, the median dose of paracetamol administered after surgery did not differ between the isoflurane group versus the sevoflurane group (P > 0.057).

These results are consistent with a study conducted by Mourad et al where the fentanyl necessary throughout the intraoperative period was less in the sevoflurane group, this could be one cause for the early eye opening in this group[41]. The results of this study are also similar to results obtained by Venkatesh et al, where the amount of top-up fentanyl dose was much more in group II (isoflurane) (265 μg± 36) than group I (sevoflurane) (150 ± 36 μg, P < 0.001)[31].

This outcome is contrary to that of Searle NR et al, who found similarity between the two gases in regards to fentanyl doses and effect of hemodynamics. The Department of Anesthesia, Montreal Heart Institute, Quebec, Canada stated that the pre-CPB use of intravenous fentanyl was not different between groups. There was a similar decrease in hemodynamic variables in both groups after induction which continued during the pre-CPB period. Pre-CPB myocardial ischemia, use of vasoactive drugs and adverse hemodynamic events did not change between groups[51]. This finding is also contrary to previous studies like the study conducted by Sahu et al, where the time of first postoperative analgesia, pain score, and adverse effects, after extubation are alike in both groups; median ± IQR in

Group I was 53.0±19 min while in Group S it was 54.5±15 min. The Mann-Whitney test analysis showed an unimpressive P value of 0.094 [45] .

5.4 Complications post open heart surgery between sevoflurane and isoflurane anesthesia.

Another important, clinically relevant finding was that patients in the isoflurane group reported significantly more complications post-operation than those in the sevoflurane group.

The current study found complications post open heart surgery in patients given sevoflurane and isoflurane as anesthetic agents. There was no significant difference regarding the prevalence of arrhythmias through or post open heart surgery among the two groups. Atrial fibrillation (AF) was seen in the isoflurane group in five (7.9%) patients, and in two patients (3.2%) in sevoflurane group (P = 0.226). Furthermore, no significant differences were noted in the type and incidence of complications regarding bleeding or CVA. Bleeding post open heart surgery was seen in five (7.9%) patients who were on isoflurane, and in three patients (4.8%) who were receiving sevoflurane (P = 0.372). CVA was reported in two patients (3.2%) in the isoflurane group and zero patients in the sevoflurane group (P = 0.254). On the other hand, nausea and vomiting occurred in nine (14.3%) patients who were administered isoflurane, but in only two (3.2%) patients who were administered sevoflurane (P = 0.026).

In a 2012 Turkish study comparing preconditioning in cardiac surgery with TIVA, sevoflurane, and isoflurane anesthesia, the incidence of arrhythmias after cross-clamp release was the same between the three groups. In the TIVA group, ventricular fibrillation (VF) was observed in 10 patients (58.8%), and seven patients (41.1%) were defibrillated. In the sevoflurane group, VF was observed in 12 patients (60%) and eight patients (40%) were defibrillated. Finally, in the isoflurane group, 11 patients (55%) were diagnosed with VF, and seven patients (35%) needed defibrillation [52]. The results of our study are in agreement with those of Frink et al, where sevoflurane induction tended to be smoother and was correlated with fewer challenges than isoflurane induction [35]. These findings are also similar with those by Dinesh et al, the study which aimed to evaluate isoflurane and sevoflurane as maintenance anesthetic agents in day care surgeries. There was no notable difference between both groups nausea and vomiting was low in both groups [50].

This study has been unable to demonstrate what Karlsen et al, did about recovery and postoperative nausea and vomiting after breast surgery. In a comparison between desflurane, sevoflurane and isoflurane anesthesia, Desflurane had a significantly higher 24 h PONV rate than isoflurane. Early PACU PONV rate was significantly ($P<0.05$) lower for the more soluble isoflurane (4%) than for the low soluble gases, desflurane and sevoflurane together (28%) [44].

5.5 Limitations and Strengthens

The first limitation that we faced during this study is the absence of BIS "By index spectral," the device which is connected to the front of the patient and detects the percentage of sedation status for the patient. It is valuable for determining the exact dose of hypnotic drug necessary for the patient to be fully sedated. The presence of this device would help making the study more accurate and exact.

The number of patients during the four months was 63, if the number of patients that met the criteria we determined for our study was higher, our results would be more accurate and exact; this is the second limitation we faced during this study.

The third limitation is the center itself, the center we chose is the only one that uses both gases, sevoflurane and isoflurane, in Palestine. The other centers use sevoflurane in less percentage than the Arab center, and they do not use sevoflurane throughout all the operation period because sevoflurane is more expensive than isoflurane. This limited the number of patients that could be included in the study.

This study is considered to be the first one of its kind in Palestine and one of the few studies around the world, as inhalation Gases is considered to be modern and new. Therefore, the studies and research are limited in this field. This is a strength point for our study.

5.6 Conclusions

The study findings show that patients receiving sevoflurane for on-pump coronary vascular surgery were safer through and post open heart surgery in sevoflurane anesthesia more than patients receiving isoflurane for the same intervention. Sevoflurane has the capacity to provide stable cardiovascular conditions through operation and a better HR profile in patients undergoing selective surgery in comparison to isoflurane volatile anesthetics. This study evaluated the hemodynamic parameters pre, through and post open heart surgery between the isoflurane and sevoflurane groups. SBP values were much lower in the isoflurane group compared to the sevoflurane group at the time of induction, opening the sternum, and once the sternum was closed; diastolic blood pressure values were much lower in the isoflurane group compared to the sevoflurane group at the time of induction, opening the sternum, and once the sternum was closed. In conclusion, the results reflect that sevoflurane has a better impact on hemodynamic stability than isoflurane. Sevoflurane produces better results in regards to systolic and diastolic pressure, HR, recovery time, ICU stay, analgesia dosage and muscle relaxant dosage. Sevoflurane usage results in less complications than isoflurane, but not significantly.

5.7. Recommendations

1- Need to have more patients and cardiac surgery centers involved in order to have a more accurate and comprehensive study. This study did not include a large number of patients because of the shortage of cases and the center that was used in the study was the only center which met the necessary criteria. More participation is needed in order to decrease bias and other factors, like the way that the anesthesiologist works, and the way that the surgeon does the operation, these factors lead to many differences in the study.

2- Use of more advanced devices in the study, like "BIS," which controls the drugs that is used in anesthesia, this device is unavailable in our cardiac surgery centers, and its presence would make the study more reliable and accurate.

3- Encouraging the use of sevoflurane rather than isoflurane in spite of its expensive price because of its benefits and advantages for patients undergoing cardiac surgeries.

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Appendix (1) data collection form

This study was designed to Clinical Comparison between Isoflurane and Sevoflurane in Patients with Open-Heart Surgery, with the knowledge that this information will be used for the purposes of scientific research and will be treated strictly confidential.

Data abstraction sheet

Name:---------------------------

_ *Data of admission:--------------------------- Data of discharge----------------*

_ Total duration in hospital ------------------------------------

_ *Hospital registration number:-----------------------*

_ *Personal information, Age:------------Years*

Gender (male , female)

History :

_*Smoking (yes , no) ,*

Number of Cigarettes------------.

_*Type of job-------------.*

_*Body mass index (   ) , High ----------------   Wight---------------*

_*History of disease:*

Name of disease	*Yes*	*No*
Diabetes mellitus		
Hypertension		
Rheumatic arthritis		

Other disease: --.

_ *medication pre-operation :*

1 ____________________________*

*2*____________________________.*

*3*_____________________________.*

*4*_____________________________.*

*5*_____________________________.*

*History of old surgery (Yes , NO)**

Name of surgery: ---.

_*Type of gases uses: (isoflurane , sevoflurane)*

_ *Time of operation: start*------------------------ *End Operation* ----------

_Time applied CVP-------------------- Time start cardiac surgery ------------------

_ Total time anesthesia procedure -----------------------------

_*Time on artificial heart and lunges (pumpest time)*-------------------*minute,hour.-*

_start pumpest------------------------------ End pumpest---------------------------------

_ *Any complication of operation:*

Type of complication	*Yes*	*NO*
Bleeding		
Cerebral vascular attack (CVA)		
Cardiogenic shock		
Multi -organ failure		
Renal failure		

Arrhythmia	*Yes*	*NO*

Type of Arrhythmia: ---.

**Other complication: -- ---.-*

1-

_ *Time of intubation -------------------- Time of extubation---------------*

_*Total time of intubation ---------------------hours-minute*

_ *Recovery time -:--*

Time admission CCU room -----------------open eyes time --
Extubation Time -----------------

_ patient post op nausea or vomiting (yes , no)

_ *Analgesia used intra* operation:

Type of analgesia	Dose	Total amount	Rote of administration
Fentanyl			

_ *Muscle relaxant used intra* operation*:*

muscle relaxant	Dose	Total Amount	Yes	No
vecuronium				

_ *Analgesia used post operation until extubation:*

Name of analgesia	*Yes*	*NO*	*Rote of administrate (IM,IV)*	*Dose*
Paracetamol intra Venus				
Morphine				

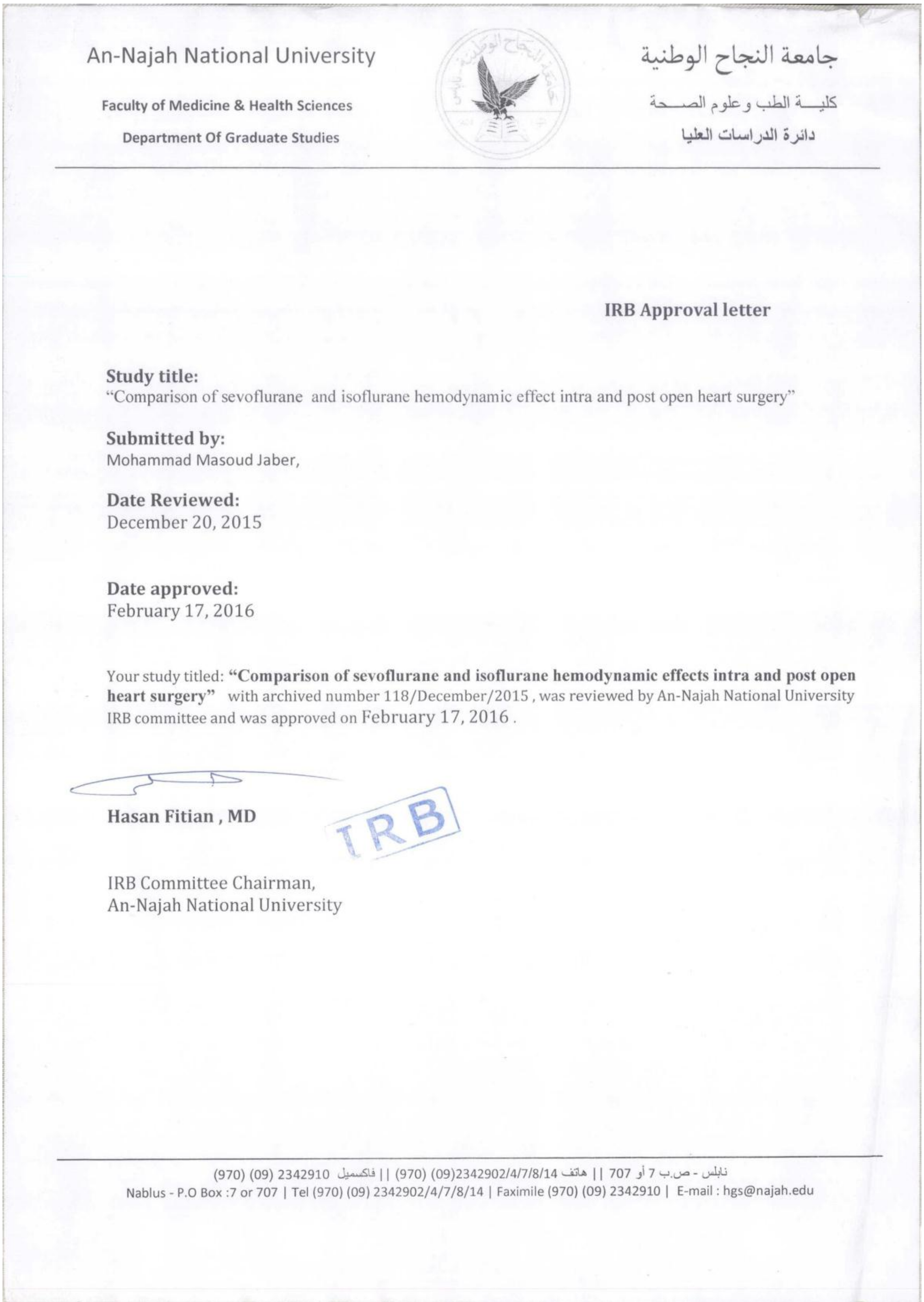
_ Vasopressors used through operation and post operation surgery:

Name of Vasopressors	Dose	Total amount	Time (total time)
Epinephrine			
Nor-epinephrine			
Nitroglycerine			

Vital signs-Hemodynamic

TIME	*PRE-OP*	*INDUCTION ANESTHESIA*	after *Open-Sternum*	*Through Closed sternum*	*After admission Ccu room*	*After extubation*
Bp						
HR						
RR						
O2 SAT						
CI						
CV						
FIO2%						

Appendix (2) IRB Approval Letter



An-Najah National University

Faculty of Medicine & Health Sciences

Department Of Graduate Studies

جامعة النجاح الوطنية

كليـــة الطب وعلوم الصـــحة

دائرة الدراسات العليا

IRB Approval letter

Study title:
"Comparison of sevoflurane and isoflurane hemodynamic effect intra and post open heart surgery"

Submitted by:
Mohammad Masoud Jaber,

Date Reviewed:
December 20, 2015

Date approved:
February 17, 2016

Your study titled: **"Comparison of sevoflurane and isoflurane hemodynamic effects intra and post open heart surgery"** with archived number 118/December/2015, was reviewed by An-Najah National University IRB committee and was approved on February 17, 2016.

Hasan Fitian, MD

IRB

IRB Committee Chairman,
An-Najah National University

نابلس - ص.ب 7 أو 707 || هاتف 2342902/4/7/8/14(09) (970) || فاكسميل 2342910 (09) (970)

Nablus - P.O Box :7 or 707 | Tel (970) (09) 2342902/4/7/8/14 | Faximile (970) (09) 2342910 | E-mail : hgs@najah.edu

جامعة النجاح الوطنية

كلية الدراسات العليا

مقارنة سريرية بين الأيزوفلورين وسيفوفلوران لمرضى جراحة القلب المفتوح: دراسة رقابية استباقية من فلسطين

إعداد

محمد مسعود جميل جابر

إشراف

د. سائد زيود

د. نجي نزال

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

2018

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اعداد

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إشراف

د. سائد زيود

د. نجي نزال

الملخص

تعتبر امراض القلب من الأمراض الشائعة في عصرنا الحالي، ومن أمراض القلب الشائعة تصلب وتسكير الشرايين مما يتسبب بحدوث الجلطات القلبية، ويتم علاج هذة الجلطات بثلاث طرق ويعتمد ذالك على القسطرة القلبية لشرايين التاجية ،منها أولاً ما تكون علاجية تعتمد على الأدوية المميعة ،ثانيا يتم فتح التسكير عن طريق الدعامات والبالونات لفتح التسكيرات الناتجة عن الجلطة القلبية ،ثالثا يتم اجراء عمليات القلب المفتوح للمرضى الذين يعانون من عدة تسكيرات في الشرايين أو فشل تركيب دعامات والفشل في فتح التسكير. وتبرز أهمية الدراسة في المقارنة بين غاز السيفوفلوران والأيزوفلوران في معرفة الغاز الأمثل والأفضل في عمليات القلب المفتوح.

هذه الدراسة عبارة عن دراسة رقابية استباقية تم تطبيقها في المستشفى العربي التخصصي في مدينة نابلس ،خلال الفترة بين شهر نيسان وشهر اب 2016، واشتملت على المرضى الذين أجروا عمليات القلب المفتوح وتنطبق عليهم شروط الدراسة، ومنها أن لا يكون المريض يعاني من أمراض الجهاز التنفس الرئوي، امراض الكلى، والمرضى التي يتراوح اعمارهم بين 30−70 عام حتى لا يؤدي ذلك الا مفارقات ومغالطات في الدراسة لأن كبر العمر يؤثر عل نتيجة ودقة الدراسة، وتم الأعتماد على جمع المعلومات من خلال مراقبة أجهزة قياس العلامات الحيوية والمراقبة بالعين المجردة وسجلات المرضى، وتم تحليل البيانات بواسطة البرنامج الأحصائي SPSS.

أشتملت الدراسة على 63 مريض انقسم منهم 31 مريض تم استخدام غاز السيفوفلوران في عملية القلب المفتوح و32 مريض تم استخدام غاز الأيزوفلوران وتم المقارنة بين الغازين من حيث الأثار والمشاكل التي حدثت خلال وبعد عملية القلب المفتوح وتبين انه توجد فروقات بسيطة بين الغازين من حيث المشاكل التي قد تحدث خلال وبعد عملية القلب المفتوح وتبن وجود بعض الفروق البسيطة ومنها نسبة حدوث الجلطات الدماغية عند اسنخدام غاز السيفوفلوران(0%) 0 وغاز الأيزوفلوران (3.2%) 2، ونسبة حدوث نزيف اثناء وبعد أجراء العملية لغاز السيفوفلوران (3.2%)2 وغاز الأيزوفلوران (7.9%) 5، وايضا نسبة حدوث عدم انتظام في ضربات القلب لغاز السيفوفلوران(3.2%) 2 وغاز الأيزوفلوران (7.9%)5، ونسبة التقيء بعد العملية لغاز السيفوفلوران(3.2%) 2 وغاز الأيزوفلوران (14.3%) 9 وهي النسبة الوحيدة المرتفعة التي لها تأثير على المرضى الذين يستخدمون غاز الأيزوفلوران وبقية النسب الأخرى ليس بالنسب العالية.

وأيضا من المقارنات نسبة مكوث المريض عل أجهزة التنفس ومدى تخلص جسم المريض من تأثير مفعول غاز التخدير والفترة التي يقضيها المريض حتى يستيقظ وازالة جهاز التخدير عن المريض، هناك تشابة في نسبة مكوث المريض في غرفة العمليات وايضا التشابة في فترة وضع المريض عل القلب الصناعي وهذا يزيد من دقة الدراسة بسبب تأثير فترة المكوث بالعملية والقلب الصناعي عل المريض بشكل عام، فترة مكوث المريض على جهاز التنفس الصناعي بعد خروجة من عملية القلب المفتوح عند المرضى الذين أستخدم لهم غاز السيفوفلوران (90− 150) 120 دقيقة والمرضى الذين استخدم لهم غاز الأيزوفلوران (180−120)150 دقيقة وأيضا فترة مكوث المرضى في المستشفى بعد العملية لمرضى السيفوفلوران (6−7)7 وغاز الأيزوفلوران (7−8) 7 أيام.

ومن المقارنات ايضا العلامات الحيوية عند المريض والتي تبين بعدم وجود مفارقات بين المرضى قبل دخول العمليات وبعد الخروج من غرفة العمليات الى غرفة العناية القلبية، ولكن هناك فروق بين كلا الغازين عند البدأ بإجراء العملية وحتى الأنتهاء منها على النحو الأتي، ضغط الدم عند مرضى غاز السيفوفلوران وقت البدأ بتخدير المريض وفتح عظمة القص وتسكيرها أقل تغيرا

ومستقرة أكثر من غاز الأيزوفلوران، وأيضا نبضات القلب عند مرض السيفوفلوران تعتبر مستقرة ولا ترتفع مقارنة مع مرضى غاز الأيزوفلوران التي ترتفع فيه نبضات القلب اثناء أجراء عملية القلب المفتوح.

ومن المقارنة بين كلا مرضى الغازين نسبة استخدام الأدوية المخدرة المساعدة مثل الفنتنيل الذي يتم استخدامة مع مرضى الأيزوفلوران بنسبة (737−550)600 مايك ونسبة غاز السيفوفلوران (500−600)550 مايك وهية اقل استخداما من غاز الأيزوفلوران، وايضا من الأدوية المخدرة المورفين ونسبة استخدامة عند مرضى الأيزوفلوران (10−15)10 ومرضى السيفوفلوران (5−10)10 وهية نسبة أقل من المرضى الذين يتم استخدام غاز الأيزوفلوران في عملياتهم، وأيضا دواء النوركورون الذي يتم استخدامة لسترخاء العضلات عند ذالك المريض وأيضا هناك نسبة أختلاف بين كلا الغازين ،غاز السيفوفلوران يستخدم (12−14)12 ملغرام بينما مرضى الأيزوفلوران يستخدمون ما نسبتة (12−14)14 ملغرام، ولا يوجد أختلاف بين الغازين من حيث استخدام مسكن الأكامول الوريدي بعد العملية.

إن هذة النتائج تعكس مدى أهمية أستخدام غاز السيفوفلوران في عمليات القلب المفتوح بالمقارنة مع المرضى الذين يستخدمون غاز الأيزوفلوران بسبب أن غاز السيفوفلوران امن من أكثر الأيزوفلوران وهذا يؤثر على المرضى والعلامات الحيوية ونسبة أستخدام الأدوية المساعدة مما ينعكس على المريض وسلامته بشكل مباشر، ويعتبر استقرار العلامات الحيوية وقلة استخدام الأدوية المخدرة المساعدة له الأثر الكبير على نجاح عمليات القلب المفتوح.