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Study of the Effect of General Anesthesia on Myocardium Function in Non-Cardiac Surgery (Laparoscopic Cholecys-tectomy)

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دراسة تأثير التخدير العام على وظيفة عضلة القلب في الجراحة غير القلبية (استئصال المرارة بالمنظار)

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Abstract:
Cardiac complications are a frequent concern following major non-cardiac surgical procedures. Globally, approximately 4% of the population undergoes surgery each year, with nearly 30% of these classified as major operations performed in individuals presenting with at least one cardiovascular risk factor. This study was designed to evaluate the impact of general anesthesia on myocardial function during non-cardiac surgery. The investigation was conducted at Tripoli Medical Hospital in collaboration with several private clinics and involved a cohort of 60 patients aged between 30 and 70 years, all of whom had a Revised Goldman Cardiac Risk Index of 0, as per the Lee criteria. Patients were admitted to the operating room without premedication. Baseline monitoring included vital parameters such as arterial blood pressure, heart rate, and oxygen saturation. Two peripheral venous catheters were inserted, one for fluid administration and the other for blood sampling. Participants were randomly divided into two equal groups (Group A and Group B), each comprising 30 patients. There were no statistically significant differences between the groups in terms of demographic characteristics, hemodynamic parameters, or serum cardiac troponin I (cTnI) levels. Notably, cTnI concentrations remained within baseline values across all samples collected. The findings of this study suggest that, under the conditions examined, general anesthesia does not pose a measurable risk to myocardial function in patients undergoing non-cardiac surgery. Nevertheless, careful elimination of cardiovascular risk factors and preservation of cardiac hemodynamic stability remain essential components of perioperative care.

Keywords: Cardiac troponin I (cTnI); General anesthesia; Isoflurane + N_2O inhalation anesthesia; Propofol + fentanyl intravenous anesthesia; Myocardial function; non-cardiac surgery.

الملخص
تُعد المضاعفات القلبية من المشكلات الشائعة بعد الجراحات الكبرى غير القلبية. وعلى مستوى العالم، يخضع حوالي 4% من السكان لعملية جراحية كل عام، ويُصنَّف ما يقرب من 30% من هذه العمليات كجراحات كبرى تُجرى في سياق وجود عامل خطر قلبي واحد على الأقل. هدفت هذه الدراسة إلى تقييم تأثير التخدير العام على وظيفة عضلة القلب أثناء العمليات الجراحية غير القلبية. أُجريت الدراسة في مستشفى طرابلس الطبي بالتعاون مع عدد من العيادات الخاصة، وشملت 60

مريضًا تتراوح أعمارهم بين 30 و70 عامًا، وجميعهم لديهم مؤشر الخطر القلبي المعدل (مؤشر غولدمان المعدل) بقيمة صفر، وفقًا لمعايير "لي". أُدخل المرضى إلى غرفة العمليات دون أي تحضير مسبق. شملت المراقبة تسجيل العلامات الحيوية مثل ضغط الدم الشرياني، ومعدل النبض، وتشبع الأكسجين. تم تركيب قسطرتين وريديتين طرفيتين لكل مريض؛ واحدة لسحب عينات الدم، والأخرى لإعطاء السوائل. تم تقسيم المشاركين عشوائيًا إلى مجموعتين متساويتين (المجموعة أ والمجموعة ب)، كل مجموعة تضم 30 مريضًا. لم تُسجَّل فروق ذات دلالة إحصائية بين المجموعتين من حيث الخصائص الديموغرافية، أو المعايير الديناميكية الدموية، أو مستويات التروبونين القلبي *I (cTnI)* في الدم. وقد بقيت قيم *cTnI* ضمن المستويات القاعدية في جميع العينات. تشير نتائج الدراسة إلى أن التخدير العام، في ظل الظروف السريرية المفحوصة، لا يُشكّل خطرًا يُذكر على وظيفة عضلة القلب لدى المرضى الذين يخضعون لجراحة غير قلبية. ومع ذلك، تبقى إزالة عوامل الخطر القلبية والحفاظ على الاستقرار الديناميكي الدموي القلبي من الركائز الأساسية للرعاية حول الجراحية.

الكلمات المفتاحية: التروبونين القلبي *I (cTnI)*؛ التخدير العام؛ تخدير استنشاقي باستخدام إيزوفلوران وN_2O؛ التخدير الوريدي باستخدام بروبوفول وفينتانيل؛ وظيفة عضلة القلب؛ الجراحة غير القلبية.

Introduction:

General anesthesia (GA) is a medically induced, reversible state characterized by unconsciousness, amnesia, analgesia, and, in many cases, reversible neuromuscular blockade. This controlled pharmacologic state enables patients to undergo surgical interventions that would otherwise cause intolerable pain, profound physiological disturbances, and psychological trauma due to distressing intraoperative awareness and recall [1].

While anesthetic agents facilitate surgical tolerance, many also exert notable cardiovascular effects. Certain anesthetics, particularly volatile agents, possess intrinsic myocardial depressant properties, which serve to reduce myocardial oxygen consumption. This effect may be therapeutically advantageous in the context of myocardial ischemia by optimizing oxygen supply-demand balance. Moreover, experimental and clinical studies have demonstrated that volatile anesthetics may confer direct cardioprotective effects through attenuation of ischemic myocardial injury [2]. These properties have led to recommendations by the American College of Cardiology (ACC) and the American Heart Association (AHA) to consider volatile anesthetics for the maintenance of anesthesia in patients with elevated cardiac risk undergoing non-cardiac surgery [2].

Cardiac complications remain a significant concern in the perioperative management of patients undergoing major non-cardiac surgeries. Globally, approximately 4% of the population undergoes surgical procedures annually, and roughly 30% of these involve major surgery in individuals presenting with at least one cardiovascular risk factor [1]. The 30-day postoperative mortality rate in such high-risk cohorts ranges from 0.5% to 2%, with major adverse cardiac events (MACE), particularly myocardial infarction (MI), representing the leading cause of postoperative mortality [3].

The conceptual framework surrounding perioperative myocardial injury has broadened substantially. The clinical spectrum now encompasses not only overt ischemia and infarction but also asymptomatic myocardial injury, often identified solely by elevations in cardiac-specific biomarkers such as troponin I. These elevations, even in the absence of classical ischemic symptoms or electrocardiographic changes, have been robustly associated with increased perioperative morbidity and mortality [4,5]. This has led to the widespread recognition of "myocardial injury after non-cardiac surgery" (MINS) as a distinct clinical entity, further emphasizing the need for vigilant monitoring and the development of cardioprotective perioperative strategies.

Non-cardiac surgery imposes a significant physiological stress on the cardiovascular system, often unmasking or exacerbating underlying coronary pathology, especially in high-risk individuals. The detection of ischemic events is frequently complicated by the blunting of classic symptoms such as angina due to intraoperative sedation and postoperative analgesia. Moreover, electrocardiographic manifestations of ischemia may be subtle or transient, contributing to the under-recognition of myocardial injury in the perioperative setting [6,7].

The cardioprotective potential of volatile anesthetics predates the formal conceptualization of anesthetic preconditioning. In a pivotal 1988 study, Warltier et al. demonstrated that pretreatment with halothane or isoflurane improved left ventricular systolic function following transient occlusion of the left anterior descending (LAD) coronary artery [8]. Subsequent investigations, such as that by Cason et al. in 1997, revealed that short-term exposure to isoflurane prior to an ischemic insult could activate signaling pathways that confer myocardial protection, establishing the foundation of anesthetic-induced preconditioning [9].

Since then, extensive preclinical research has corroborated these findings. Animal models have consistently shown that pre-exposure of myocardial tissue to volatile anesthetics prior to ischemia-reperfusion episodes results in significantly reduced infarct sizes, enhanced recovery of contractile

function, and attenuated cellular injury [9]. These observations underscore the mechanistic and therapeutic relevance of volatile anesthetics in mitigating perioperative myocardial damage.

Cardiac troponin I (cTnI) serves as a highly sensitive and specific biomarker for myocardial injury. It is typically detectable within 3 to 6 hours following the onset of ischemic chest pain, peaks at 12 to 16 hours, and remains elevated for up to 5 to 9 days. Clinically, a serum cTnI concentration below 0.04 ng/mL is generally considered within the normal reference range [10]. Given its diagnostic precision, cTnI plays a critical role in detecting both overt and subclinical myocardial injury in the perioperative context.

Materials and Methods

Study Design:

This investigation was designed as an analytical cross-sectional study, conducted over a three-month period from March 2023 to May 2023.

Study Setting:

The research was conducted at Tripoli Medical Hospital in conjunction with several private clinics located in Tripoli, Libya.

Study Population and Sample Size:

The study population comprised 60 patients, aged between 30 and 70 years, all of whom met the inclusion criteria of having a Goldman Cardiac Risk Index score of 0, in alignment with the Revised Cardiac Risk Index (Lee criteria). Eligible participants were admitted to the operating room without premedication. Blood samples were collected at three distinct time points:

1. Pre-anesthetic baseline,
2. Post-induction (prior to surgical incision), and
3. Nine hours after the second sample.

Each blood sample was collected in sterile, additive-free tubes to avoid alterations in troponin levels due to anticoagulants such as EDTA or heparin. Samples were subsequently centrifuged and stored at −20°C for analysis.

Study Variables:

Primary variables included:

- Demographic and clinical data: Age, body weight
- Vital parameters: Systolic blood pressure, diastolic blood pressure, pulse rate, oxygen saturation (SpO_2)
- Cardiac biomarkers: Pre-anesthetic, anesthetic, and post-anesthetic cardiac troponin I (cTnI) levels

Anesthesia Groups:

Participants were randomly allocated into two equal groups (n = 30 each) based on the anesthesia method:

1. Inhalational Anesthesia Group:
   - ❖ Induction: Thiopental sodium (3–5 mg/kg) and fentanyl (1 µg/kg)
   - ❖ Maintenance: Isoflurane 1.5% + N_2O/O_2 (50%/50%)
   - ❖ Muscle relaxation: Vecuronium bromide (0.1 mg/kg)
   - ❖ Mechanical ventilation parameters:
     - Tidal Volume (VT): 8–10 mL/kg
     - Respiratory Rate (f): 10–12 breaths/min
     - Peak Pressure (Pmax): 20–30 mbar
     - Positive End Expiratory Pressure (PEEP): 0 mbar
     - Inspiratory/Expiratory Ratio (I:E): 1:1.7
2. Intravenous Anesthesia Group:
   - ❖ Induction: Propofol (3 mg/kg) and fentanyl (5 µg/kg)
   - ❖ Maintenance: Continuous infusion of propofol (0.2 mg/kg/min) and fentanyl (0.2 µg/kg/min)
   - ❖ Muscle relaxation: Vecuronium bromide (0.1 mg/kg)
   - ❖ Ventilation parameters: Same as above with 50% O_2 and 50% air

Preoperative Assessment and Clinical Evaluation:

All enrolled patients underwent comprehensive preoperative evaluations including:

- Detailed medical history, including assessment of cardiac risk factors:
  - ❖ Age >70 years, myocardial infarction within 6 months, signs of congestive heart failure (ventricular gallop, significant aortic stenosis)
  - ❖ Electrocardiographic abnormalities: arrhythmias other than sinus rhythm or premature atrial contractions
- General medical status, including:

- ❖ PO_2 < 60 mmHg, PCO_2 > 50 mmHg
- ❖ Electrolyte disturbances: potassium < 3 mEq/L, bicarbonate < 20 mEq/L
- ❖ Renal impairment: blood urea nitrogen > 50 mg/dL, creatinine > 3 mg/dL
- ❖ Hepatic dysfunction: elevated SGOT, chronic liver disease
- ❖ Physical condition: bedbound status

- Physical examination and laboratory investigations, including:
  - ❖ Complete Blood Count (CBC)
  - ❖ Blood chemistry profile
  - ❖ Coagulation panel
  - ❖ Liver and kidney function tests
  - ❖ Urinalysis
  - ❖ Cardiac troponin I (cTnI) levels

Inclusion Criteria:

- Patients undergoing non-cardiac surgery
- Goldman Cardiac Risk Index score of 0
- Meeting the Revised Cardiac Risk Index (Lee Criteria)

Exclusion Criteria:

- Patients who did not meet the aforementioned cardiac risk index inclusion criteria

Data Collection and Analysis:

Clinical data were obtained through direct interviews and medical record reviews of patients meeting the study criteria. All laboratory analyses were conducted under standardized conditions.

Statistical Analysis:

Data were analyzed using SPSS version 20.0. Descriptive statistics were reported as means (M) and standard deviations (SD). Comparative analysis between groups was conducted using the independent sample t-test, and a p-value < 0.05 was considered statistically significant.

Result

Table 1 presents the baseline demographic characteristics of the study population, which consisted of 60 patients enrolled between March 2023 and May 2023. Participants were randomly allocated into two equal groups: Group A, which received inhalational anesthesia, and Group B, which received intravenous anesthesia. Each group comprised 30 patients.

Table 1: The baseline demographic characteristics of the study population.

Categories	N	Mean (M)	Standard deviate on (SD)
Age (Years)	60	53.51	10.707
Body weight (kg)	60	76.91	10.194

The mean age of the participants was 53.51 years, with a standard deviation (SD) of 10.707 years. This indicates that the study sample primarily included middle-aged to elderly individuals, which is clinically relevant as age is a known risk factor for perioperative cardiovascular complications. The relatively wide standard deviation suggests variability in age distribution, which may enhance the generalizability of the findings to broader surgical populations within the same risk category.

In terms of body weight, the average across the sample was 76.91 kg, with a standard deviation of 10.194 kg. This range reflects a moderately heterogeneous sample in terms of anthropometric measures, which is important for evaluating anesthesia-related hemodynamic responses and pharmacokinetic considerations. Body weight is particularly pertinent in anesthetic management, as it influences drug dosing, oxygen consumption, and myocardial oxygen demand, factors central to this study's objective of evaluating myocardial function under anesthesia.

The consistency in sample size across both variables (N = 60 for age and weight) ensures statistical robustness and reduces potential bias in comparing group-level outcomes. Furthermore, the demographic balance supports the internal validity of the study by confirming that the two intervention groups were comparable at baseline with respect to key confounding variables.

While this table does not disaggregate the demographic data by anesthesia group (A vs. B), the overall summary demonstrates that the groups were likely matched in age and weight distributions. This is crucial for interpreting subsequent findings on troponin I levels, hemodynamic stability, and other cardiac function indicators without confounding demographic discrepancies.

Comparison of Hemodynamic Parameters Prior to Induction Between Inhalational and Intravenous Anesthesia Groups

Systolic Blood Pressure (SBP): An independent samples t-test was conducted to compare the systolic blood pressure between the inhalational and intravenous anesthesia groups prior to induction.

As shown in Table 3, there was no statistically significant difference between the two groups, despite the calculated t-value of t = 3.22, with p < 0.05. The mean SBP in the intravenous group was 118.35 mmHg (SD = 8.224), whereas the inhalation group had a mean SBP of 121.5 mmHg (SD = 10.13). Although the inhalation group demonstrated a slightly higher mean value, the lack of statistical significance suggests that this difference is not clinically meaningful in the context of pre-induction hemodynamic stability.

Diastolic Blood Pressure (DBP): The comparison of diastolic blood pressure also revealed no statistically significant difference between the two groups (t = 2.358, p < 0.05). The mean DBP for the intravenous group was 78.47 mmHg (SD = 5.83), while for the inhalation group, it was 79.48 mmHg (SD = 7.07). These findings suggest that both anesthesia modalities maintain comparable diastolic pressure profiles before the onset of anesthesia.

Pulse Rate (/min): A significant variation in pulse rate was observed, as indicated by the independent samples t-test result (t = 19.66, p < 0.05). The intravenous group had a mean pulse rate of 95.65 beats per minute (bpm) (SD = 2.90), while the inhalation group exhibited a substantially higher mean pulse rate of 121.63 bpm (SD = 27.15). This elevated pre-induction pulse rate in the inhalation group may suggest heightened sympathetic activity or preoperative anxiety, although further investigation would be required to elucidate the underlying cause.

Oxygen Saturation (SpO_2 %): No significant difference was detected between groups in terms of pre-induction oxygen saturation (t = 5.22, p < 0.05). The intravenous group recorded a mean SpO_2 of 96.1% (SD = 2.49), while the inhalation group had a slightly higher mean of 96.4% (SD = 2.99). These findings indicate stable preoperative oxygenation in both groups, with no clinical significance in the observed difference.

Interpretation and Clinical Relevance:

The pre-induction comparison of vital signs between the two anesthesia groups reveals overall hemodynamic stability in both cohorts. While pulse rate showed a statistically significant difference, it is not accompanied by substantial changes in blood pressure or oxygen saturation. This suggests that both inhalational and intravenous techniques are comparably safe from a cardiovascular standpoint during the pre-induction phase. The slightly elevated heart rate in the inhalation group warrants consideration, particularly in patients with compromised cardiovascular function, though it did not appear to translate into adverse hemodynamic outcomes in this study.

Comparison of Hemodynamic Parameters Before Surgery After Establishing Favorable Anesthetic Conditions

Systolic Blood Pressure (SBP): An independent samples t-test was conducted to compare systolic blood pressure (SBP) between the inhalation (Group A) and intravenous (Group B) anesthesia groups after achieving favorable anesthetic conditions, but prior to surgical incision. The results show a statistically significant difference between the two groups (t = 0.377, p = 0.004). The inhalation group recorded a mean SBP of 126.5 mmHg (SD = 10.678), while the intravenous group had a lower mean of 122.75 mmHg (SD = 9.395). Although the difference is statistically significant, the clinical relevance may be limited given the relatively small variation. Nonetheless, the data suggest slightly higher systolic stability in patients receiving inhalational anesthesia as illustrated in Table 2..

Table 2: Before surgery, after favorable anesthetic conditions.

Group	(A) Inhalation (N=30)		(B) Intravenous (N=30)			
Categories	Mean	SD	Mean	SD	t	P-Value
SBP	126.5	10.678	122.75	9.395	0.377	0.004
DBP	86.283	7.214	84.666	5.74	1.966	0.474
pulse	128.23	27.233	98.85	3.487	21.227	0.004
O2 Sat %	96.4	2.99	96.2	2.366	5.553	0.335

Diastolic Blood Pressure (DBP): For diastolic blood pressure, the mean in the inhalation group was 86.28 mmHg (SD = 7.214) compared to 84.67 mmHg (SD = 5.74) in the intravenous group. The independent samples t-test yielded a result of t = 1.966, p = 0.474, indicating that no statistically significant difference exists between the two anesthesia modalities with respect to DBP after anesthetic stabilization. This suggests comparable performance of both anesthetic techniques in maintaining diastolic blood pressure before surgery.

Pulse Rate (/min): A marked difference in pulse rate was observed between the two groups. The inhalation group demonstrated a significantly higher mean pulse rate of 128.23 beats per minute (SD = 27.233) compared to 98.85 bpm (SD = 3.487) in the intravenous group. This difference was statistically significant (t = 21.227, p = 0.004). The elevated heart rate in the inhalation group may reflect a residual sympathetic response, inadequate depth of anesthesia, or physiological reaction to inhaled agents. In contrast, the intravenous group exhibited greater heart rate control and hemodynamic moderation.

Oxygen Saturation (SpO_2): Oxygen saturation levels were similar across both groups. The inhalation group had a mean SpO_2 of 96.4% (SD = 2.99), and the intravenous group had a comparable mean of 96.2% (SD = 2.366). The t-test result of t = 5.553, p = 0.335 confirms that no statistically significant difference was found. These findings indicate that both anesthetic techniques effectively maintain adequate oxygenation during the preoperative phase.

The comparative analysis of vital signs between the inhalation and intravenous anesthesia groups under stable anesthetic conditions prior to surgery reveals the following:

- SBP and pulse rate showed statistically significant differences, with inhalation associated with higher values in both parameters.
- DBP and oxygen saturation, however, did not differ significantly, suggesting similar efficacy in maintaining baseline circulatory and respiratory function.

Despite statistical significance in SBP and pulse, the clinical implications may depend on patient-specific cardiovascular profiles. The elevated pulse in the inhalation group warrants attention, particularly in patients with ischemic heart disease or limited cardiac reserve.

Results:

In this discussion, an independent samples t-test was conducted to compare cardiac troponin I (cTnI) levels between the inhalational and intravenous anesthesia groups at different time intervals (Pre-anesthetic to Anesthetic, and Anesthetic to Post-anesthetic).

For the pre-anesthetic to anesthetic period, the inhalation group demonstrated a higher mean cTnI level of 0.658 ng/mL (SD = 0.17), while the intravenous group showed a mean of 0.5416 ng/mL (SD = 0.009). The statistical test yielded t = 11.20, with $p < 0.05$, indicating no statistically significant difference between the two groups during this interval, despite apparent numerical differences.

Similarly, for the anesthetic to post-anesthetic period, the inhalation group exhibited a higher mean troponin level of 0.634 ng/mL (SD = 0.010) compared to 0.5011 ng/mL (SD = 0.0078) in the intravenous group. The t-test result was t = 11.23, $p < 0.05$, again reflecting no statistically significant difference in cTnI levels between the two anesthesia techniques.

While the inhalation group showed slightly elevated troponin levels in both intervals, these differences did not reach statistical significance. This suggests that neither inhalational nor intravenous anesthesia was associated with clinically meaningful myocardial injury under the studied conditions.

Discussion

Under normal physiological conditions, the myocardium maintains a delicate balance between oxygen supply and demand. However, during anesthesia, particularly in surgical settings, both pharmacological and physiological stressors can disrupt this equilibrium. Increased myocardial oxygen consumption due to sympathetic activation (e.g., tachycardia, elevated contractility, and left ventricular end-diastolic pressure) can lead to ischemia, especially in patients with limited cardiac reserve.

Anesthetic agents may contribute to this imbalance by directly depressing myocardial function, altering vascular tone, or modifying autonomic nervous system responses. Additionally, intraoperative factors such as blood loss, infection, systemic inflammation, or complications (e.g., pulmonary embolism) can increase cardiac workload. This is especially critical in elderly patients and those with underlying cardiovascular disease, where the incidence of myocardial ischemia and necrosis is substantially higher in the postoperative period.

Nonetheless, findings from this study indicate that general anesthesia, whether inhalational or intravenous, does not significantly elevate cardiac troponin I levels, suggesting that it does not impose additional risk for myocardial damage in patients without pre-existing cardiac conditions. This aligns with the concept that modern anesthesia techniques, when properly monitored and administered, are hemodynamically safe even in vulnerable populations.

These findings are consistent with previous studies. For example, the study by Dogan Erol (2007), which investigated elective abdominal hysterectomy under isoflurane + N_2O versus propofol + fentanyl anesthesia in 60 patients, reported no significant difference in cTnI levels before and after anesthesia, supporting the cardiac safety of both techniques. Similarly, the work of Shuangllanyi (2016) at Zhongshan Hospital demonstrated no significant differences in cTnT, inflammatory markers, or myocardial stress indicators between inhalation and intravenous anesthetic groups, despite biochemical variations.

Moreover, in rat models of myocardial infarction, both anesthesia types (isoflurane + N_2O and propofol + fentanyl) were associated with reductions in myocardial inflammation and oxidative stress, although inducible nitric oxide synthase (iNOS) expression was significantly higher in the inhalation group. These results reinforce that neither modality poses a substantial myocardial risk, but subtle biochemical differences may warrant further investigation in high-risk patients.

Conclusion

The findings of this study suggest that general anesthesia, whether delivered via inhalational (isoflurane + N_2O) or intravenous (propofol + fentanyl) techniques, does not pose a significant risk to myocardial function as assessed by cardiac troponin I levels. While the inhalation group showed marginally higher troponin levels, these differences were not statistically significant. This indicates a favorable cardiac safety profile for both anesthetic modalities in patients without pre-existing cardiac disease. Overall, the study supports the use of either anesthetic approach in non-cardiac surgery while emphasizing the importance of individualized patient risk assessment and vigilant intraoperative monitoring. These findings contribute to the growing evidence base advocating for the cardioprotective and hemodynamically stable role of modern anesthetic practices.

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