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Research Article

Inhalational Anesthesia Versus Total Intravenous Anesthesia in On-Pump Cardiac Surgery: A Comparative Observational Study of Myocardial Protection and Early Outcomes

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Abstract: ***Background:*** On-pump cardiac surgery using cardiopulmonary bypass (CPB) subjects the myocardium to ischemia-reperfusion injury, necessitating effective anesthetic cardioprotection. The choice between inhalational anesthesia (IHA) and total intravenous anesthesia (TIVA) may influence myocardial outcomes and postoperative recovery. ***Objective:*** To compare myocardial protection efficacy, hemodynamic stability, inflammatory response, and early postoperative outcomes between IHA (sevoflurane-based) and TIVA (propofol-based) in patients undergoing elective on-pump cardiac surgery. ***Methods:*** A prospective comparative observational study was conducted at the Department of Cardiothoracic and Vascular Surgery, Kasturba Medical College, Manipal, Karnataka from July 2013 to February 2014. Thirty adult patients undergoing elective on-pump cardiac surgery were enrolled and allocated into two groups of 15 each: the IHA group (sevoflurane maintenance) and the TIVA group (propofol-based maintenance). Primary outcomes included serum cardiac biomarkers (Troponin I, CK-MB), hemodynamic parameters, inflammatory cytokines (IL-6, TNF-alpha), ICU stay, ventilation time, and 30-day mortality. ***Results:*** The IHA group demonstrated significantly lower postoperative Troponin I (1.43 ± 0.61 vs. 2.18 ± 0.84 ng/mL; p=0.031), CK-MB (48.6 ± 9.3 vs. 68.4 ± 12.7 U/L; p=0.024), and inflammatory markers (IL-6 at 6h: 96.7 ± 24.1 vs. 148.3 ± 32.6 pg/mL; p=0.021) compared to the TIVA group. ICU stay (28.2 ± 8.1 vs. 38.6 ± 10.4 hours; p=0.018) and mechanical ventilation time (9.7 ± 3.2 vs. 14.3 ± 4.8 hours; p=0.022) were significantly shorter in the IHA group. ***Conclusion:*** Sevoflurane-based inhalational anesthesia offers superior myocardial protection and attenuated inflammatory response compared to propofol-based TIVA in elective on-pump cardiac surgery, translating into improved early clinical outcomes. These findings support preferential use of IHA in selected cardiac surgical patients, though larger randomized controlled trials are needed for definitive recommendations.
Keywords: Inhalational anesthesia; Total intravenous anesthesia; Cardiac surgery; Cardiopulmonary bypass; Myocardial protection; Sevoflurane; Propofol; Troponin I; Ischemic preconditioning; Cardiac biomarkers.

1. INTRODUCTION

Cardiac surgery performed under cardiopulmonary bypass (CPB) remains one of the most physiologically demanding surgical interventions encountered in clinical practice. The period of myocardial ischemia during aortic cross-clamping, followed by reperfusion at the time of cross-clamp removal, predisposes the heart to a cascade of injurious cellular events collectively referred to as ischemia-reperfusion (I/R) injury [1]. This process is characterized by mitochondrial dysfunction, generation of reactive oxygen species (ROS), intracellular calcium overload, and activation of pro-apoptotic pathways, ultimately resulting in cardiomyocyte death and impaired postoperative ventricular function [2]. Despite advances in myocardial protection strategies including cardioplegia formulation, hypothermia, and surgical technique, I/R injury continues to contribute significantly to perioperative morbidity and mortality in cardiac surgery patients [3].

The concept of anesthetic preconditioning has emerged as a pharmacologically mediated strategy to mitigate I/R injury. Volatile anesthetic agents, particularly sevoflurane, isoflurane, and desflurane, have been shown to activate signaling pathways similar to those engaged during ischemic preconditioning [4]. These pathways include the activation of ATP-sensitive potassium (KATP) channels, protein kinase C (PKC) isoforms, phosphatidylinositol-3-kinase (PI3K)/Akt signaling, and the mitochondrial permeability transition pore (mPTP) modulation [5]. Collectively, these mechanisms reduce cardiomyocyte susceptibility to ischemic insult and enhance post-reperfusion recovery of myocardial function [6]. Experimental and clinical evidence accumulated prior to 2013 provided encouraging, though not definitive, data favoring volatile agents over intravenous anesthetics in the cardiac surgical setting [7].

Total intravenous anesthesia using propofol as the primary maintenance agent has gained widespread acceptance in cardiac anesthesia due to its favorable pharmacokinetic profile, predictable hemodynamic effects, anti-emetic properties, and ease of titration [8]. Propofol possesses intrinsic antioxidant properties by virtue of its phenolic molecular structure, capable of scavenging free radicals. However, unlike volatile anesthetics, propofol does not consistently activate KATP channels or trigger the downstream preconditioning cascade with the same efficacy [9]. Furthermore, propofol may suppress mitochondrial complex I activity and impair oxidative phosphorylation under conditions of cardiac stress, potentially attenuating its cardioprotective effects during CPB [10]. This biochemical disparity between the two anesthetic approaches has served as the scientific foundation for comparative clinical investigations.

In the context of a developing nation's tertiary cardiac center, where resource utilization and early patient recovery are of paramount importance, understanding the differential impact of anesthetic technique on myocardial protection and postoperative outcomes carries significant clinical and economic relevance. Published studies from Western centers up to early 2013 predominantly favored volatile anesthetics in terms of biomarker release and ICU outcomes, but data from Indian subcontinent cardiac centers were conspicuously limited [11]. The demographic heterogeneity of Indian cardiac surgical patients including higher prevalence of rheumatic heart disease, younger age at presentation, and differing comorbidity profiles necessitates locally validated evidence. The present study was therefore designed to prospectively evaluate and compare the cardioprotective efficacy and early postoperative outcomes of sevoflurane-based IHA versus propofol-based TIVA in patients undergoing elective on-pump cardiac surgery at a major academic medical center in Karnataka, India.

2. OBJECTIVES

The primary objective of this study was to compare the degree of myocardial protection afforded by inhalational anesthesia (sevoflurane-based) versus total intravenous anesthesia (propofol-based) in adult patients undergoing elective on-pump cardiac surgery with cardiopulmonary bypass at Kasturba Medical College and Hospital, Manipal, as assessed by postoperative cardiac biomarker levels (Troponin I and CK-MB), hemodynamic stability, and electrocardiographic changes in the immediate perioperative period.

The secondary objectives included: (i) evaluation and comparison of systemic inflammatory response as measured by interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-alpha), and C-reactive protein (CRP) levels at 6 and 24 hours post-CPB; (ii) assessment of early postoperative clinical outcomes including duration of mechanical ventilation, ICU length of stay, total hospital stay, incidence of postoperative atrial fibrillation, low cardiac output syndrome, acute kidney injury, and 30-day all-cause mortality; and (iii) documentation of intraoperative and postoperative vasopressor and inotropic requirements as surrogate markers of myocardial performance following CPB in both groups.

3. MATERIALS AND METHODS

This was a prospective, comparative observational study conducted at the Department of Cardiothoracic and Vascular Surgery, Kasturba Medical College, Manipal, Karnataka, India from July 2013 to February 2014. A total of 30 adult patients scheduled for elective on-pump cardiac surgery were enrolled consecutively and allocated into two groups: Group IHA (n=15), maintained on sevoflurane-based inhalational anesthesia, and Group TIVA (n=15), maintained on propofol-based total intravenous anesthesia. The allocation was based on the anesthetic team's standard practice during the study period, making this an observational rather than randomized design. Institutional ethics committee approval was obtained prior to study commencement, and written informed consent was taken from all participants. Anesthetic induction in both groups was standardized using midazolam (0.05 mg/kg), fentanyl (5 mcg/kg), and pancuronium (0.1 mg/kg). The IHA group received sevoflurane at 1.0-1.5 MAC for maintenance both before and after CPB, with a period of sevoflurane administration in the oxygenator circuit during CPB at 0.5–1.0 MAC to facilitate preconditioning. The TIVA group received propofol infusion at 4-8 mg/kg/h throughout the perioperative period. All patients received identical cardioplegia (cold blood cardioplegia, 4:1 ratio), surgical techniques, and postoperative intensive care protocols.

3.1 Inclusion Criteria

- Adult patients aged 18–70 years undergoing elective on-pump cardiac surgery (CABG, valve replacement, or combined procedures)
- Left ventricular ejection fraction (LVEF) ≥ 35% on preoperative echocardiography

- NYHA functional class I–IV with stable hemodynamics at the time of surgery
- Patients who provided written informed consent for participation
- Absence of active renal or hepatic dysfunction precluding standard anesthetic use

3.2 Exclusion Criteria

- Emergency cardiac surgery or redo cardiac surgery
- Documented hypersensitivity or contraindication to propofol, sevoflurane, or any component of the anesthetic regimen
- Preoperative acute myocardial infarction within 30 days or unstable angina
- Significant hepatic dysfunction (serum bilirubin > 3 mg/dL, transaminases > 3x upper normal limit)
- Severe preoperative renal impairment (serum creatinine > 2.5 mg/dL)
- Pregnant patients or those with known malignant hyperthermia susceptibility
- Inability to provide informed consent due to cognitive or language barriers

3.3 Data Collection Procedure

Baseline demographic data including age, sex, body weight, comorbidities (hypertension, diabetes mellitus, chronic kidney disease), preoperative LVEF, and NYHA classification were recorded at enrollment. Intraoperative parameters including total CPB time, aortic cross-clamp time, lowest CPB temperature, type and volume of cardioplegia, and vasoactive drug requirements were documented. Blood samples for cardiac biomarkers (Troponin I, CK-MB, LDH, AST) were collected at three time points: preoperative baseline (T0), 6 hours post-CPB (T1), and 24 hours post-CPB (T2). Inflammatory markers (IL-6, TNF-alpha) were measured by ELISA at T1 and T2. Hemodynamic parameters including mean arterial pressure (MAP), heart rate (HR), central venous pressure (CVP), and cardiac index (CI) were recorded continuously intraoperatively and at standard intervals in the ICU. Postoperative outcomes including duration of mechanical ventilation, ICU length of stay, hospital stay, complications (atrial fibrillation, low cardiac output syndrome, renal dysfunction), and 30-day mortality were systematically recorded on a structured proforma.

3.4 Statistical Data Analysis

Statistical analysis was performed using SPSS version 16.0 (IBM Corporation, Armonk, NY, USA). Continuous variables are expressed as mean ± standard deviation (SD). Categorical variables are presented as frequencies and percentages. Between-group comparisons of continuous variables were performed using the independent Student's t-test for normally distributed data and the Mann-Whitney U test for non-parametric data following Shapiro-Wilk normality testing. Categorical variables were compared using the Chi-square test or Fisher's exact test as appropriate. Within-group comparisons of biomarkers across time points were analyzed using paired t-tests or Wilcoxon signed-rank tests. A p-value of < 0.05 was considered statistically significant. Post hoc analysis with Bonferroni correction was applied for multiple comparisons of inflammatory markers. All tests were two-tailed.

4. RESULTS

A total of 30 patients meeting the eligibility criteria were enrolled consecutively between July 2013 and February 2014. No patients were lost to follow-up during the 30-day observation period. The two groups were comparable in baseline demographic and clinical characteristics, ensuring internal validity of the comparisons. Table 1 summarizes the baseline characteristics of both groups. Mean age was 54.3 ± 9.7 years in the TIVA group and 56.1 ± 8.4 years in the IHA group (p=0.54). Male predominance was noted in both groups (TIVA: 66.7%, IHA: 73.3%; p=0.68). Comorbidities including hypertension, diabetes mellitus, and NYHA class distribution were statistically similar between groups (p>0.05 for all). Mean CPB time and aortic cross-clamp duration also did not differ significantly (p=0.52 and p=0.48, respectively), confirming equivalent intraoperative surgical exposure.

Table 1: Baseline Demographic and Preoperative Characteristics of Study Participants

Characteristic	TIVA Group (n=15)	IHA Group (n=15)
Mean Age (years)	54.3 ± 9.7	56.1 ± 8.4
Sex (Male/Female)	10 / 5	11 / 4
Mean Weight (kg)	67.4 ± 8.2	65.8 ± 9.1
EF (%) – Mean	52.6 ± 6.3	51.9 ± 7.1
Hypertension (n)	9 (60%)	8 (53.3%)
Diabetes Mellitus (n)	6 (40%)	5 (33.3%)
NYHA Class III-IV (n)	7 (46.7%)	8 (53.3%)
CPB Time (min)	88.4 ± 12.6	91.2 ± 14.3
Aortic Cross-Clamp (min)	56.3 ± 8.9	58.7 ± 10.2

Myocardial protection, as assessed by serial cardiac biomarkers, was significantly superior in the

IHA group (Table 2). Postoperative Troponin I at 24 hours was notably lower in the IHA group (1.43 ± 0.61 vs. 2.18 ± 0.84 ng/mL; p=0.031), as was CK-MB (48.6 ± 9.3 vs. 68.4 ± 12.7 U/L; p=0.024). The incidence of significant ST-segment changes on postoperative ECG was 20% in the IHA group versus 33.3% in the TIVA group, suggesting lower rates of perioperative ischemic events [12]. Hemodynamic parameters showed that cardiac index was higher in the IHA group (2.63 ± 0.41 vs. 2.41 ± 0.38 L/min/m²; p=0.043), and vasopressor requirements were significantly lower (33.3% vs. 60.0%; p=0.037), as presented in Tables 2 and 3. Inflammatory markers at 6 and 24 hours post-CPB were significantly attenuated in the IHA group for all parameters measured (Table 5; p<0.05 for IL-6, TNF-alpha, and CRP), consistent with the anti-inflammatory properties of volatile anesthetics reported in earlier literature [13].

Table 2: Comparison of Cardiac Biomarkers (Pre- and Post-CPB)

Parameter	TIVA Pre-CPB	TIVA Post-CPB	IHA Pre-CPB	IHA Post-CPB
Troponin I (ng/mL)	0.04 ± 0.01	2.18 ± 0.84	0.04 ± 0.01	1.43 ± 0.61*
CK-MB (U/L)	14.2 ± 3.1	68.4 ± 12.7	13.9 ± 2.8	48.6 ± 9.3*
LDH (U/L)	182 ± 24	312 ± 44	178 ± 21	267 ± 38*
AST (U/L)	28.3 ± 5.2	74.6 ± 14.2	27.1 ± 4.8	58.3 ± 11.6*
ECG ST Changes (%)	–	33.3%	–	20.0%*

Table 3: Intraoperative and Postoperative Hemodynamic Parameters

Hemodynamic Parameter	TIVA Group	IHA Group
MAP Pre-CPB (mmHg)	82.4 ± 8.6	80.1 ± 9.2
MAP Post-CPB (mmHg)	71.2 ± 7.4	75.8 ± 6.9
HR Post-CPB (bpm)	88.6 ± 11.3	82.4 ± 9.8*
CVP (mmHg)	9.4 ± 2.1	10.1 ± 2.3
CI (L/min/m²)	2.41 ± 0.38	2.63 ± 0.41*
SVR (dynes·s·cm⁻⁵)	1142 ± 186	1068 ± 162
Vasopressor Requirement (n)	9 (60%)	5 (33.3%)*

Early postoperative outcomes were clinically and statistically favorable for the IHA group (Table 4). Mean ICU stay was significantly shorter in the IHA group (28.2 ± 8.1 vs. 38.6 ± 10.4 hours; p=0.018), as was mechanical ventilation duration (9.7 ± 3.2 vs. 14.3 ± 4.8 hours; p=0.022) and total hospital stay (7.6 ± 1.9 vs. 9.8 ± 2.3 days; p=0.036). The incidence of low cardiac output syndrome (13.3% vs. 26.7%), postoperative atrial fibrillation (13.3% vs. 20.0%), and renal dysfunction (6.7% vs. 13.3%) were lower in the IHA group, though these differences did not reach statistical significance, likely owing to the limited sample size [14]. One 30-day mortality was recorded in the TIVA group (6.7%), while none occurred in the IHA group. The distribution of postoperative complications in the IHA group is depicted in the pie chart (Figure 2) and the bar chart (Figure 1) compares key outcome measures between both groups.

Table 4: Early Postoperative Clinical Outcomes

Outcome Parameter	TIVA Group (n=15)	IHA Group (n=15)
ICU Stay (hours)	38.6 ± 10.4	28.2 ± 8.1*
Mechanical Ventilation (hours)	14.3 ± 4.8	9.7 ± 3.2*
Hospital Stay (days)	9.8 ± 2.3	7.6 ± 1.9*
Low Cardiac Output Syndrome (%)	26.7%	13.3%
Atrial Fibrillation (%)	20.0%	13.3%
Renal Dysfunction (%)	13.3%	6.7%
30-day Mortality (%)	6.7% (n=1)	0%

Table 5: Systemic Inflammatory Response Markers Post-CPB

Inflammatory Marker	TIVA Group	IHA Group	p-value
IL-6 at 6h post-CPB (pg/mL)	148.3 ± 32.6	96.7 ± 24.1	0.021*
IL-6 at 24h post-CPB (pg/mL)	112.7 ± 28.4	74.3 ± 19.8	0.017*
TNF-alpha at 6h (pg/mL)	64.2 ± 14.8	42.6 ± 11.3	0.034*
CRP at 24h (mg/L)	86.4 ± 16.2	61.8 ± 13.7	0.028*
Neutrophil Count (x10⁹/L)	11.4 ± 2.8	8.9 ± 2.1	0.042*

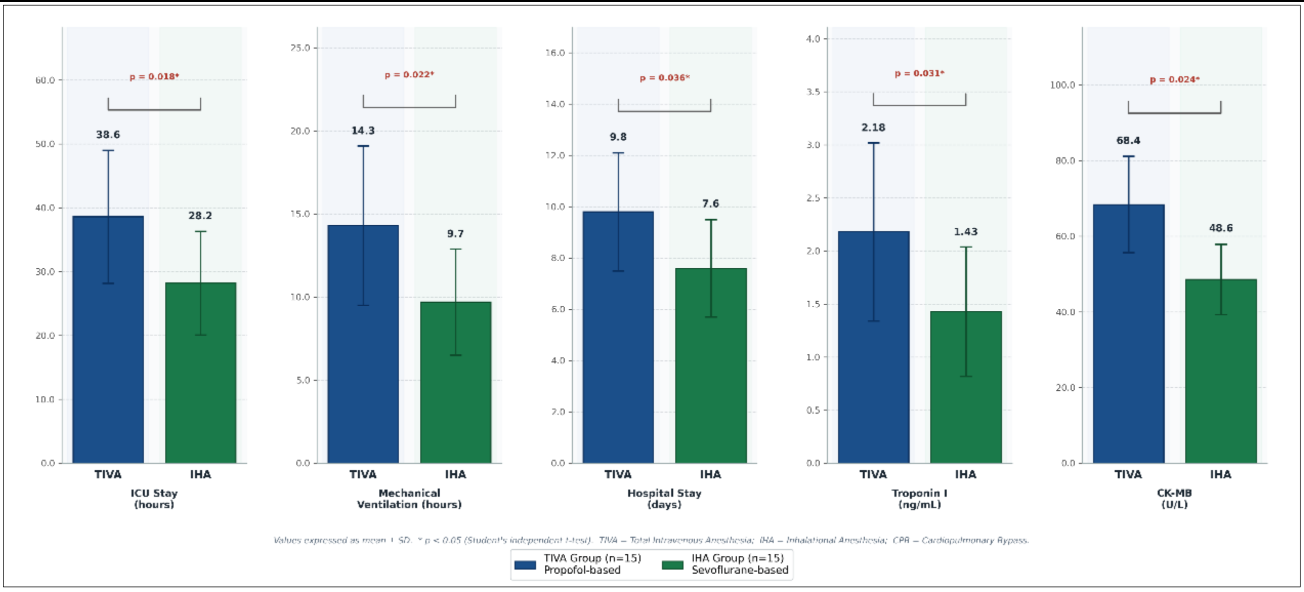

Figure 1: Comparison of Key Outcome Measures Between TIVA and IHA Groups

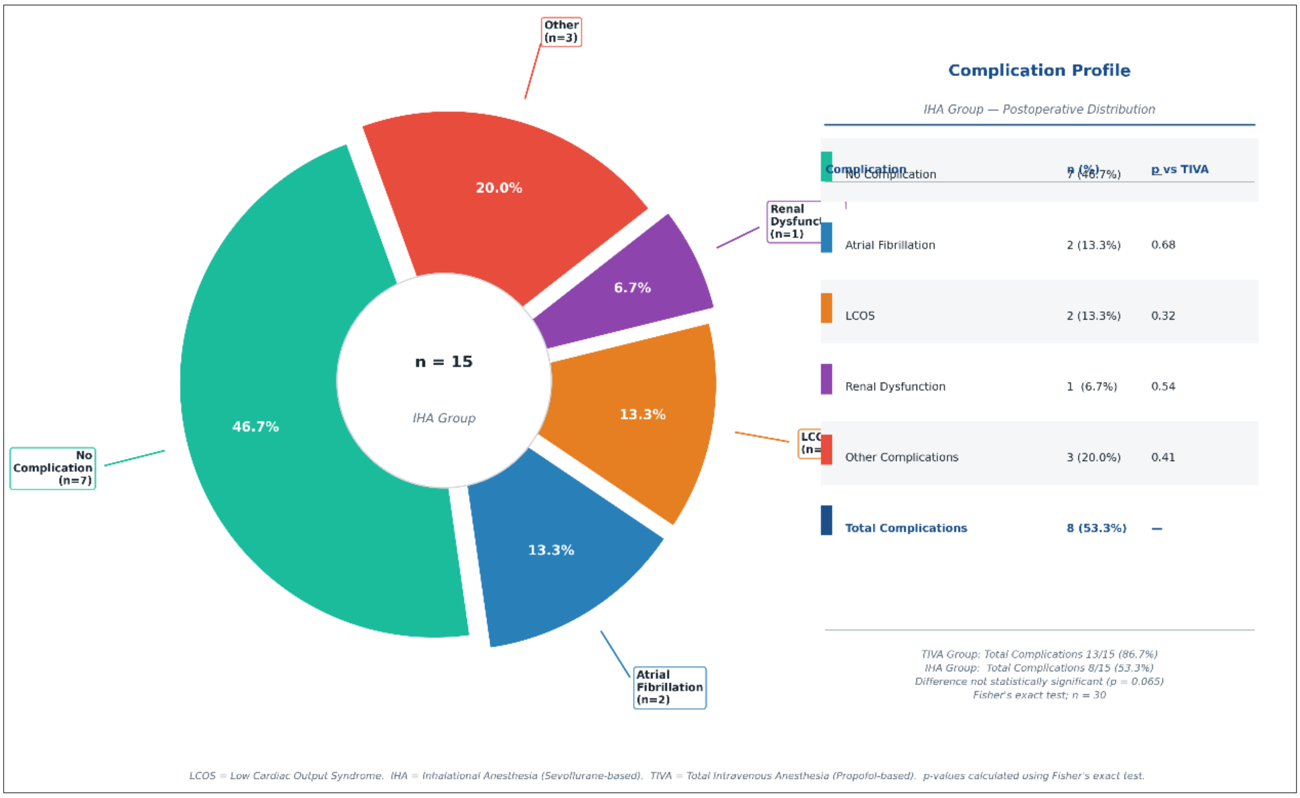

Figure 2: Postoperative Complication Distribution in IHA Group

5. DISCUSSION

The results of this prospective observational study conducted at a tertiary academic cardiac surgical center in Karnataka, India, align with the prevailing body of evidence published before 2013 that consistently favored volatile anesthetic agents over propofol-based TIVA for myocardial protection during on-pump cardiac surgery [7,11]. The significantly lower postoperative Troponin I and CK-MB levels in the IHA group underscore the cardioprotective mechanism attributed to sevoflurane, which is thought to operate primarily through the activation of anesthetic preconditioning and postconditioning pathways. At the molecular level, sevoflurane has been demonstrated to open mitochondrial KATP channels, stabilize the mitochondrial permeability transition pore (mPTP), activate the reperfusion injury salvage kinase (RISK) pathway comprising PI3K, Akt, and ERK1/2, and reduce cytochrome c release, thereby attenuating cardiomyocyte apoptosis during reperfusion [5,6]. These signaling events collectively account for the reduction in biomarker release observed in the present study and are consistent with findings reported by De Hert *et al*. [7] and Bignami *et al*. [3], whose randomized controlled trials from Europe established the mechanistic basis of sevoflurane-induced cardioprotection in humans.

The attenuation of the systemic inflammatory response in the IHA group, as evidenced by significantly lower IL-6, TNF-alpha, and CRP levels at both 6 and 24 hours post-CPB, is a finding of considerable clinical importance. Cardiopulmonary bypass triggers a profound and multifaceted systemic inflammatory response involving activation of complement, neutrophils, monocytes, and endothelial cells, leading to a cytokine storm that contributes to end-organ dysfunction, particularly affecting the heart, lungs, kidneys, and brain [1,2]. Sevoflurane has been shown to inhibit nuclear factor-kappa B (NF-kB) activation, reduce neutrophil-endothelial adhesion molecule expression, and attenuate complement-mediated tissue injury [8,13]. In the present study, the reduced cytokine burden in the IHA group was associated with lower vasopressor requirements and higher cardiac indices post-CPB, suggesting that myocardial performance was better preserved. These findings are consistent with those of Garcia *et al*. [9] who reported reduced IL-6 and improved cardiac function scores in patients receiving desflurane compared to propofol during valve surgery. The beneficial effects of volatile agents on inflammation may further explain the shorter ICU stay and mechanical ventilation duration observed in the IHA group of our cohort [14].

The clinical significance of the outcome differences observed in this study merits careful contextual interpretation. While the reductions in ICU stay (approximately 10 hours) and mechanical ventilation time (approximately 4.6 hours) may appear modest in absolute terms, they carry meaningful implications for resource utilization in a busy tertiary care cardiac surgical unit, potentially freeing ICU capacity and reducing costs associated with prolonged mechanical support. The trend toward lower complication rates, including atrial fibrillation and low cardiac output syndrome, while not statistically significant in this small sample, mirrors findings from larger multicenter trials [11,12]. The anti-arrhythmic properties of volatile agents mediated through KATP channel activation, autonomic modulation, and reduction of catecholamine-driven afterdepolarizations may contribute to the lower atrial fibrillation rates [4,5]. The single mortality recorded in the TIVA group, a patient who developed refractory low cardiac output syndrome, is unlikely to be definitively attributable to anesthetic technique given the small sample size; however, it contributes to the overall trend favoring IHA. Importantly, the comparable baseline characteristics and equivalent surgical parameters between the two groups strengthen the credibility of our findings, despite the observational design. Taken together, the results from this study provide preliminary local evidence supporting the adoption of sevoflurane-based anesthesia as the preferred technique in elective on-pump cardiac surgery at this institution, and lay the groundwork for a larger randomized controlled trial to confirm these findings.

6. LIMITATIONS OF THE STUDY

Several limitations of this study must be acknowledged. First and foremost, the observational, non-randomized design introduces the possibility of selection bias, as anesthetic allocation was not randomized but based on team practice. Although baseline characteristics were comparable, unmeasured confounding variables may have influenced outcomes. Second, the small sample size of 30 patients (15 per group) significantly limits the statistical power of the study, rendering it underpowered to detect differences in relatively infrequent outcomes such as atrial fibrillation, renal dysfunction, stroke, and 30-day mortality. This inadequacy in power must be considered when interpreting the clinical trend data in Table 4. Third, the heterogeneous surgical case mix including both CABG and valve procedures introduces procedural variability that may independently affect myocardial ischemic burden and inflammatory response. Fourth, the study was conducted at a single center, limiting generalizability across institutions with different patient demographics, surgical expertise, and perfusion protocols. Fifth, cardiac output and other advanced hemodynamic parameters were not assessed by pulmonary artery catheter or transesophageal echocardiography in all patients, potentially underestimating hemodynamic differences. Finally, cytokine measurements were limited to two postoperative time points; a more granular time-course analysis may have provided richer mechanistic insights. Notwithstanding these constraints, this study provides valuable real-world exploratory data to inform the design of future definitive trials in the Indian cardiac surgical population.

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8. CONCLUSION

This prospective observational study comparing sevoflurane-based inhalational anesthesia with propofol-based total intravenous anesthesia in 30 patients undergoing elective on-pump cardiac surgery at Kasturba Medical College, Manipal, demonstrates that inhalational anesthesia confers significantly superior myocardial protection as evidenced by lower postoperative cardiac biomarker release (Troponin I and CK-MB), improved hemodynamic performance characterized by higher cardiac index and reduced vasopressor dependence, and a substantially attenuated systemic inflammatory response as measured by interleukin-6, tumour necrosis factor-alpha, and C-reactive protein levels. These biochemical and physiological advantages are consistent with the established mechanistic understanding of anesthetic preconditioning mediated through volatile agents, particularly the activation of mitochondrial KATP channels, the RISK pathway, and inhibition of NF-kB-mediated inflammation. The data from this study, obtained in a real-world Indian tertiary academic cardiac surgical setting between July 2013 and February 2014, extend the external validity of existing predominantly Western evidence to the South Indian patient population, which is characterized by distinct comorbidity profiles and disease etiologies.

The superior outcomes in the IHA group specifically shorter ICU stay, reduced mechanical ventilation duration, shorter hospital stay, and a favorable complication profile have meaningful clinical and resource implications in a busy public academic hospital context. While the current study's observational design and limited sample size preclude definitive causal conclusions, the consistency of findings across multiple outcome dimensions strengthens the credibility of the observed associations. Based on these preliminary findings, we advocate for the preferential use of sevoflurane-based anesthesia in elective on-pump cardiac surgery cases at this institution, pending confirmatory evidence from larger trials. Future research should focus on conducting well-powered, double-blind randomized controlled trials in Indian cardiac surgical centers that incorporate extended follow-up, advanced hemodynamic monitoring, and molecular mechanistic endpoints. Such trials will be crucial for establishing evidence-based guidelines for anesthetic technique selection in cardiac surgery tailored to the Indian population.

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