# Effectiveness of high-flow inhalation anesthesia technique using isoflurane compared to low-flow inhalation anesthesia technique

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Original Article

# Effectiveness of High-flow Inhalation Anesthesia Technique Using Isoflurane Compared to Low-flow Inhalation Anesthesia Technique Using Sevoflurane and Isoflurane in Terms of Cost and Safety

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## Abstract

**Background:** The low-flow technique could reduce the direct and indirect total cost as well as lower the pollution and glasshouse effects. This study aimed to compare the effectiveness of two inhalation anesthetic agents using low-flow techniques on the hemodynamic changes and cost needed. **Subjects and Methods:** This is an experimental study with posttest-only control group design and a cost minimization analysis on sixty patients, who had underwent surgery and met the inclusion and exclusion criteria. Patients were grouped into high-flow isoflurane (HIS), low-flow isoflurane (LIS), and low-flow sevoflurane (LSV) groups. The amount of anesthetic agent used was measured before and after the surgery. The cost needed was the main outcome of this research. **Results:** There was no significant difference in the hemodynamic changes between these three groups ($P > 0.05$). There was a significant cost difference between the three groups ($P = 0.003$). There was no significant cost difference between LIS and LSV groups ($P = 0.353$). There was a significant difference between the cost of high flow and low flow, but there was no significant difference between the cost of low-flow anesthetic agents. **Conclusion:** HIS resulted in a more expensive compared to the LIS and LSV. However, there was no significant cost difference between the use of low-flow techniques.

**Keywords:** Anesthetic, cost, hemodynamic, inhalation, isoflurane, sevoflurane

## Introduction

Advancement in technology and monitoring technique in anesthesia allowed the low-flow technique to be used worldwide. The low-flow technique could reduce the direct and indirect total costs as well as lower the pollution and glasshouse effects.[1-4] Many studies also showed that it is more effective to reduce the use of fresh gas flow (FGF) in anesthesia education program to contribute to the reduction of total anesthetic cost.[5]

There are three steps in applying the low-flow anesthesia (LFA) technique: initial high-flow stage, low flow, and recovery. The initial high-flow stage is performed in 10–20 min using 4 L/min FGF (i.e., 1.4 L/min $O_2$ and 3 L/min $N_2O$) with the aim to achieve desirable anesthetic gas composition within the respiratory system.[2] The LFA technique is more favorable because the use of FGF ≤1 L/min can still achieve the depth of anesthesia desired without unwanted glasshouse side effects and the cost required is lower.[2-4] Routine use of low-flow technique can reduce anesthesia cost up to 75%.[6]

There are three components regarding the cost of anesthesia procedure. First is the direct cost from the drugs or anesthetic agents, anesthetic machine, and the executor of the anesthetic procedure. Indirect cost is the consequence of anesthetic procedure (i.e., postoperative care in the intensive care unit or long observation in recovery room). Unexpected cost is for postoperative pain management and consequences of the surgery itself.[1] Inhalation anesthetic agents play a vital role in the cost of anesthetic drugs.

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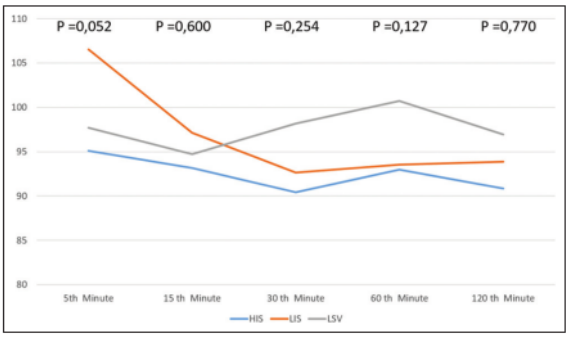


**Figure 1:** Mean arterial pressure differences between each group. LSV: Low-flow sevoflurane, LIS: Low-flow isoflurane, HIS: High-flow isoflurane

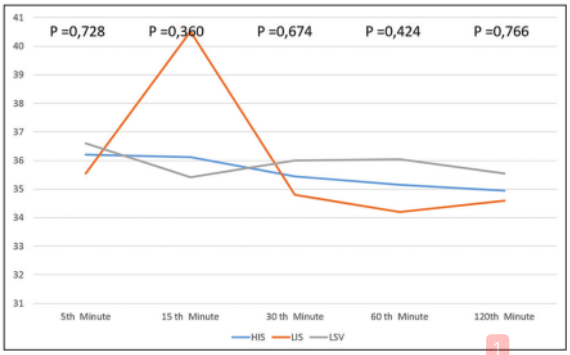


**Figure 2:** $EtCO_2$ differences between each group. LSV: Low-flow sevoflurane, LIS: Low-flow isoflurane, HIS: High-flow isoflurane

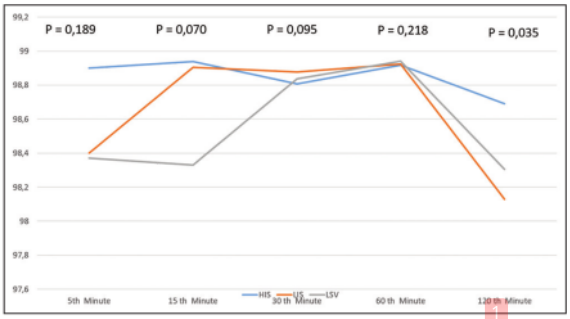


**Figure 3:** $SpO_2$ differences between each group. LSV: Low-flow sevoflurane, LIS: Low-flow isoflurane, HIS: High-flow isoflurane

Isoflurane and sevoflurane are anesthetic agents most commonly used as inhalation agents.[1] There are four reasons why they are expensive. First, the anesthetic agent is available in liquid form, and the price is costed per milliliter of the liquid. Second, the gas volume produced by 1 ml of the liquid. Third, the price of the components needed to produce its capacity are different among each agent, and it is affected by the agent's concentration produced by the vaporizer to reach the anesthesia depth needed for each patient (vol%). Fourth, the price of anesthetic agents wasted.[1] A survey done by Cotter *et al.*[7] showed that routine LFA use can minimize the cost of inhalation agent.

This study aimed to compare the effectiveness of two inhalation anesthetic agents using low-flow and high-flow techniques on the hemodynamic changes and cost needed. The objectives of this research were to analyze the hemodynamic changes that could happen using low-flow techniques compared to high-flow techniques, and whether there were significant cost differences between the low-flow techniques.

## Subjects and Methods

This study is an experimental study with posttest-only control group design and a cost minimization analysis, comparing the hemodynamic changes and operational cost from an alternative anesthetic technique equivalent to the operational cost of the anesthetic technique regularly used. This study protocol has been approved by the institutional review board. Informed consent was obtained from each patient.

This study took 3 months with sixty patients who met the inclusion and exclusion criteria and randomized into three groups. The first group received inhaled general anesthesia with high-flow technique using 50% air in oxygen with 4 L/min FGF dan isoflurane. The second group received inhaled general anesthesia with low-flow technique using 50% air in oxygen with 1 L/min FGF dan isoflurane. The third group received inhaled general anesthesia with low-flow technique using 50% air in oxygen with 1 L/min FGF dan sevoflurane.

During anesthesia, hemodynamic parameters including mean arterial pressure (MAP), heart rate, $SpO_2$, and $EtCO_2$ were measured every 5 min. After the surgery, the anesthetic cost was calculated from each group. Data processing was performed using the Statistical Packages for the Social Sciences software 21.0 IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp. Data were analyzed using the Kruskal–Wallis and Mann–Whitney tests to measure the cost difference between the groups. ANOVA and Kruskal–Wallis test were used to analyze the hemodynamic changes, duration of surgery, and anesthetic agent used between the groups of high-flow isoflurane (HIS), low-flow isoflurane (LIS), and low-flow sevoflurane (LSV). $P > 0.05$ was considered statistically significant.

## Results

The patients from the three groups were compared demographically [Table 1]. The participants of this study were sixty patients who were distributed proportionally into three groups. The total sample consisted of 23 male patients and 37 female patients. Demographic characteristics of this research were age, gender, American Society of Anesthesiologists physical status, and body mass index. The sample distribution was tested statistically using the Kolmogorov–Smirnov test, which showed normally distributed.

**Table 1: Demographic characteristics of the patients in each group**

| Variables | HIS | LIS | LSV | *P* |
|---|---|---|---|---|
| Age (years), mean±SD | 37.67±11.87 | 44.25±15.57 | 43.10±11.63 | 0.138 |
| Gender, *n* (%) | | | | |
| Male | 9 (45) | 9 (45) | 5 (25) | 0.197 |
| Female | 11 (55) | 11 (55) | 15 (75) | |
| ASA PS, *n* (%) | | | | |
| 1 | 6 (30) | 11 (55) | 6 (30) | 1 |
| 2 | 14 (70) | 9 (45) | 14 (70) | |
| BMI (kg/m$^2$), mean±SD | 24.81±2.21 | 24.35±2.7 | 23.15±2.8 | 0.3 |
| Surgical duration (h), mean±SD | 3.31±1.55 | 3.40±1.08 | 4.02±1.54 | 0.231 |
| Amount of anesthetic agent used (mL), mean±SD | 57.1±36.2 | 39.15±30.81 | 37.55±14.65 | 0.013 |
| Anesthesia agent cost (USD), mean±SD | 15.16±9.63 | 10.39±8.18 | 12.39±4.84 | 0.021 |

LSV: Low-flow sevoflurane, LIS: Low-flow isoflurane, HIS: High-flow isoflurane, ASA: American Society of Anesthesiologists, BMI: Body mass index, SD: Standard deviation, PS: Physical status

The mean equilibration time in HIS, LIS, and LSV groups were 3.31 ± 1.55, 3.40 ± 1.08, and 4.02 ± 1.54 h, respectively ($P$ = 0.231). The mean anesthetic agent used in HIS, LIS, and LSV groups were 57.1 ± 36.2, 39.15 ± 30.81, and 37.55 ± 14.65 mL, respectively ($P$ = 0.013). Hemodynamic parameters were measured since the agent was used until the surgery finished. Monitoring was carried out on the 5$^{th}$, 15$^{th}$, 30$^{th}$, 60$^{th}$, and 120$^{th}$ min. There was no significant difference in MAP, EtCO2, and SpO2 between these groups [Figures 1-3].

The mean anesthesia cost of the LIS group was USD 10.38 ± 8.17. The highest anesthesia cost in this group was USD 42.41, and the lowest anesthesia cost in this group was USD 2.65. The mean anesthesia cost of the LSV group was USD 12.37 ± 4.83. The highest anesthesia cost in this group was USD 24.71 and the lowest anesthesia cost in this group was USD 6.59. The result of statistical analysis using ANOVA test for these three groups showed a significantly different result ($P$ = 0.003), whereas the statistical analysis between LIS and LSV showed an insignificant result ($P$ = 0.353).

## Discussion

The usage of sevoflurane as inhalation agent needs to be limited because it is relatively more expensive than other anesthetic agents. The variety duration of operation in this research was in accordance with the daily operation cases that met by all anesthesiologists in the hospital. Statistical analysis of the operation length showed an insignificant result ($P$ = 0.231), which means there were no significant differences between the duration of operation for each group. We can conclude that the duration of operation would not have any impact on the anesthetic cost.

Some studies in American and European countries that compared anesthesia cost between LSV and HIS showed varieties of results due to their differences in anesthesia procedures and equipment.[1-10] The use of LFA technique could prevent the excessive amount of anesthesia cost. In 2005–2006, the Nebraska Medical Center reported that using LFA, they saved up to USD 477,000.[11] One study concluded that inhalation anesthesia with 0.5 L/min compared to 6 L/min in 1000 h of anesthesia could save up to 600% of the cost. Inhalation anesthesia technique using 0.5 L/min could reduce the halothane cost up to USD 1000 and isoflurane cost up to USD 9100.[12]

Our hospital's anesthetic cost was measured by the sum of the used anesthetic agent and the price of rented anesthetic equipment (excluding oxygen and vaporizer). The result of this study showed that the mean cost of the HIS group was USD 15.16 compared to the LIS group (USD 10.39) and LSV (USD 12.39). A comparative study using ANOVA test resulted in $P$ = 0.021 in these three groups, which indicates a statistically significant difference between these groups.

In this study, we also measured the hemodynamic changes in these three groups, especially the $EtCO_2$ changes. Using the LFA technique would increase the risk of rebreathing that could cause a raise in blood $CO_2$ concentration. In this study, the mean result of $EtCO_2$ was within the normal limit. The statistical analysis of the $EtCO_2$ difference between these three groups was statistically insignificant. MAP changes in these three study groups also showed an insignificant result ($P$ > 0.05). Previous research in patients with prior reduced renal function showed that there were not any statistical differences between sevoflurane and isoflurane in terms of drug safety.[13,14]

## Conclusion

There was no significant difference in the hemodynamic changes between the high-flow and low-flow techniques. LIS was as effective as LSV in maintaining hemodynamic status. However, there was a significant cost difference between the three groups. HIS resulted in a more expensive compared to the LIS and LSV. However, there was no significant cost difference between the use of low-flow techniques.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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