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# Cost minimization analysis of hypnotic drug: Target Controlled Inhalation Anesthesia (TCIA) sevoflurane and Target Controlled Infusion (TCI) propofol



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Made Wiryana,<sup>1</sup> I Gusti Ngurah Mahaalit Aribawa,<sup>2\*</sup> Tjokorda Gde Agung Senapathi,<sup>3</sup>  
I Made Gede Widnyana,<sup>4</sup> I Gusti Agung Gede Utara Hartawan,<sup>5</sup> Made Agus Kresna  
Sucandra,<sup>6</sup> Pontisomaya Parami,<sup>7</sup> Kadek Agus Heryana Putra,<sup>8</sup> IB Krisna Jaya Sutawan,<sup>9</sup>  
IGNA Putra Arimbawa,<sup>10</sup> Ketut Semara Jaya,<sup>11</sup> Gede Semarawima<sup>12</sup>

## ABSTRACT

**Background:** Cost minimization analysis is a pharmaco-economic study used to compare two or more health interventions that have been shown to have the same effect, similar or equivalent. With limited health insurance budget from the Indonesian National Social Security System implementation in 2015, the quality control and the drug cost are two important things that need to be focused. The application of pharmaco-economic study results in the selection and use of drugs more effectively and efficiently.

**Objective:** To determine cost minimization analysis of hypnotic drug between a target controlled inhalation anesthesia (TCIA) sevoflurane and a target controlled infusion (TCI) propofol in patients underwent a major oncologic surgery in Sanglah General Hospital.

**Methods:** Sixty ASA physical status I-II patients underwent major oncologic surgery were divided into two groups. Group A was using

TCIA sevoflurane and group B using TCI propofol. Bispectral index monitor (BIS index) was used to evaluate the depth of anesthesia. The statistical tests used are the Shapiro-Wilk test, Lavenne test, Mann-Whitney U test and unpaired t-test ( $\alpha = 0.05$ ). The data analysis used the Statistical Package for Social Sciences (SPSS) for Windows.

**Results:** In this study, the rate of drug used per unit time in group A was 0.12 ml sevoflurane per minute ( $\pm 0.03$ ) and the group B was 7.25 mg propofol per minute ( $\pm 0.98$ ). Total cost of hypnotic drug in group A was IDR598.43 (IQR 112.47) per minute, in group B was IDR703.27 (IQR 156.73) per minute ( $p > 0.05$ ).

**Conclusions:** There was no statistically significant difference from the analysis of the drug cost minimization hypnotic drug in a major oncologic surgery using TCIA sevoflurane and TCI propofol.

**Keywords:** Hypnotic drug, cost minimization analysis, TCIA sevoflurane, TCI propofol

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## INTRODUCTION

In the healthcare reformation era, it is important to be able to demonstrate some economical values of a new technology. Healthcare reformation also put more pressure for anesthesiologist to determine the cost impact of anesthesia strategies, drugs and technologies.<sup>1-7</sup>

High cost of anesthesia has always been a problem in the hospital management. As pharmacology and technology advance, there are various anesthesia techniques and the development of anesthesia depth monitoring tools which could assist anesthesiologist in determining the drug using and appropriate dosages. The development of computerized systems and availability of short acting drugs such as propofol and sufentanyl, made the target controlled infusion (TCI) increasingly used for total intravenous anesthesia.<sup>8</sup> Anesthesia inhalation technique has been making progress as well, with a low fresh gas flow 2 liter per minute (lpm) and

target controlled inhalational anesthesia (TCIA) with end tidal (ET) control which is a conductive anesthesia system available in newer anesthesia machine. It is a kind of anesthetic gas conductor system, in which the machine would automatically adjusts the concentration of anesthetic agents to achieve the desired target level set by the user.<sup>9-11</sup>

We were determined to do a research on cost minimization analysis of hypnotic drug used for general anesthesia with manually controlled TCIA sevoflurane and TCI propofol in Sanglah General Hospital 2016.

## METHODS

This study is an experimental design with non-blind randomized controlled trial. The clinical trials were conducted on 60 patients who met the eligibility criteria who underwent mastectomy surgery and thyroidectomy in Sanglah General Hospital from January to March 2016.

<sup>1</sup>Professor,  
<sup>2-10</sup>Lecturer,

<sup>11</sup>Head of Medical Service Division,  
<sup>12</sup>Resident Anesthesiology and Intensive Care Department, Udayana University, Sanglah General Hospital, Denpasar, Bali, Indonesia

\*Correspondence to: I Gusti Ngurah Mahaalit Aribawa, MD, Anesthesiology and Intensive Care Department, Udayana University, Sanglah General Hospital, Denpasar, Bali  
mahaalit@unud.ac.id

The inclusion criteria are: (1) admitted in our hospital from January to March 2016, (2) ASA physical status I-II, (3) 16-64 years old by the time of the admission, (4) the body height is more or equal to 130 cm, (5) the body mass index is 18.5 kg/m<sup>2</sup> - 24.5 kg/m<sup>2</sup>, (6) willing to undergo surgery with general anesthesia technique TCIA sevoflurane or total intravenous use of TCI propofol by signing the informed consent, (7) the patient uses one of the following insurance as a mean of payment: National Health Insurance (JKN), *Bali Mandara* Health Insurance, Health Insurance for the Poor (JAMKESMAS), Indonesian National Social Security System (BPJS).

The exclusion criteria are: (1) the patient refused to participate as a research subject, (2) the bleeding during the surgery >30% Estimated Blood Volume, (3) duration of surgery <1 hour, (4) allergic to propofol, (5) allergic to sevoflurane, (6) patients with hypovolemic shock, (7) has a psychiatric disorder, (8) presents neurological deficits (9) has a heart and blood vessels disease and have experienced a cerebrovascular event.

The sample was taken using a consecutive sampling technique. They were divided into two groups by randomized blocks: 30 people in one group received a general anesthesia TCIA sevoflurane, and 30 others in another group received a general anesthesia TCI propofol. The participants flow details are available in [Chart 1](#) and [Chart 2](#). An analysis of cost comparison was also conducted between TCIA sevoflurane and TCI propofol. The data analysis used the Statistical Package for Social Sciences for Windows (SPSS Inc., Chicago, version 20.0).

## RESULTS

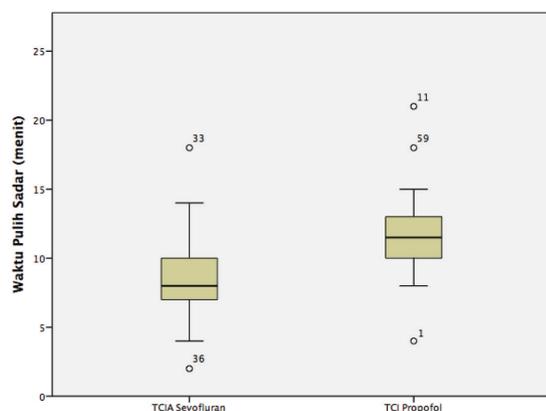
The age in both groups are normally distributed. The age in the TCIA sevoflurane group ranged from 22-63 years, with an average of 47.7 years (SD 9.9). The age in the TCI propofol group ranged from 31-63 years, with an average of 51.6 years (SD 7.8). Based on the gender, the TCIA sevoflurane group consists of 8 men and 22 women (26.7% and 73.3% respectively). The TCI propofol group consists of 5 men and 25 women (16.7% and 78.3% respectively). Based on the ASA physical status, the TCIA sevoflurane group consists of 11 ASA I (36.7%) and 19 ASA II (63.3%), while the TCI propofol group consists of 8 ASA I (26.7%) and 22 ASA II (73.3%). Based on the Body Mass Index (BMI), the TCIA sevoflurane group ranged from 19.1 to 24.8 kg/m<sup>2</sup>, with an average of 22.2 kg/m<sup>2</sup> (SD 1.8). The BMI in the TCI propofol group ranged from 17.9 to 24.5 kg/m<sup>2</sup>, with an average of 21.7 kg/m<sup>2</sup> (SD 1.9). Based on the type of the surgery, the TCIA

**Table 1** Comparison of The Duration of Surgery, The Duration of Anesthesia and The Total Drug Used

	Group	
	TCIA Sevoflurane	TCI Propofol
	n=30	n=30
Duration of surgery (minutes, IQR)	202.00 (73)	195.50 (61)
Duration of anesthesia (minutes, IQR)	233.50 (81)	230.00 (71)
<b>Total Drug Used</b>		
Sevoflurane (ml ± SD)	29.06 ± 8.30	
Propofol (mg ± SD)		1723.50 ± 474.93
<b>Ratio of drug used per unit of time</b>		
Sevoflurane (ml/minute ± SD)	0.12 ± 0.03	
Propofol (mg/minute ± SD)		7.25 ± 0.98

**Table 2** Comparison of Hypotensive Incidents Post-induction Between The Two Groups

Side Effects	Group		p
	TCIA Sevoflurane n=30 f(%)	TCI Propofol n=30 f(%)	
Hypotensive Incident	6 (20%)	5 (16.7%)	0.739



**Figure 1** Comparison of Recovery Time between The Two Groups (axis: time of recovery in minutes)

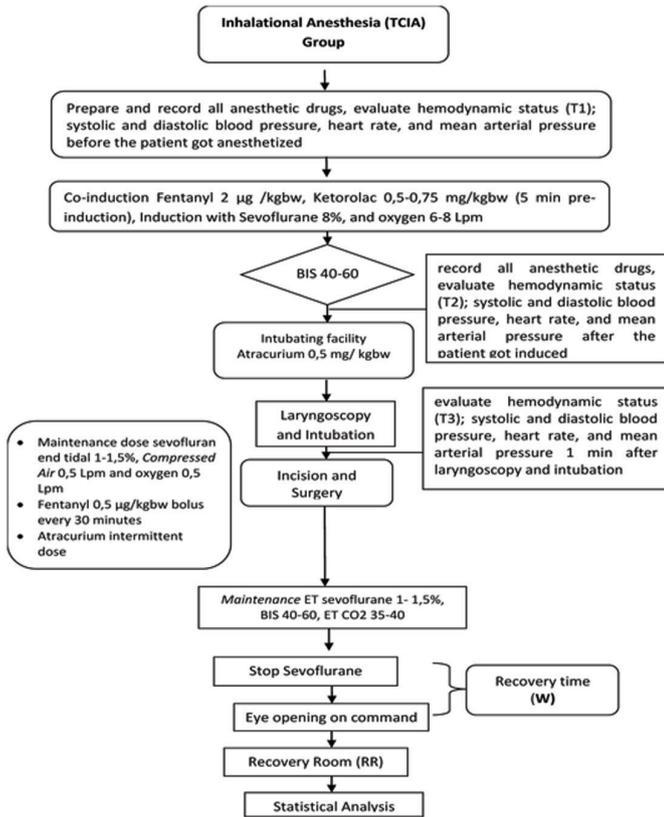


Chart 1

The TCIA Participants Flow

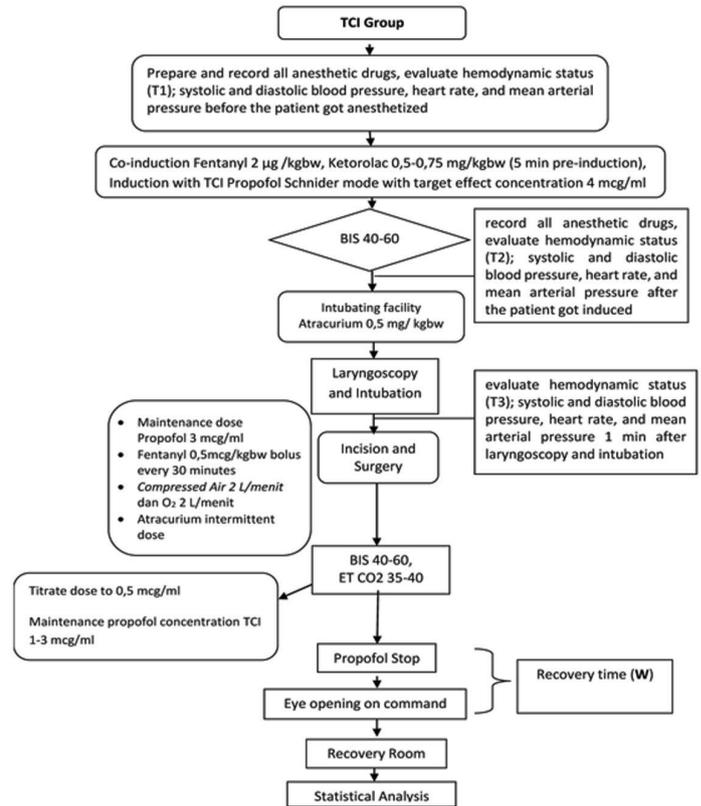


Chart 2

The TCI Participants Flow

Table 3 Comparison of The TCIA Sevoflurane and The TCI Propofol Costs

	Group		P
	TCIA Sevoflurane n=30 in IDR (IQR)	TCI Propofol n=30 in IDR (IQR)	
Cost	152,360 (70,320)	187,038 (41,564)	0.146
Cost per minute of hypnotic drug	598,43 (112.47)	703,27 (156.73)	0.138

sevoflurane group consists of 17 people underwent mastectomy (56.7%) and 13 people underwent thyroidectomy (43.3%). While in the TCI propofol group, 18 people underwent a mastectomy (60%) and 12 thyroidectomies (40%).

An adverse event recorded in both groups was post-induction hypotension. The incidence of other side effects such as agitation, nausea, vomiting, bronchospasm, cough, bradycardia and tachycardia did not occur. In the TCIA group the incidence of hypotension occurred was 20.0% (n=6), whereas in the TCI propofol group was 16.75% (n=5). Table 2 shows there is no significant difference between the two groups (p=0.739), based on the Pearson chi-square test.

Figure 1 shows the median recovery time in the TCIA sevoflurane group was 8 minutes, faster than the median recovery time in the TCI propofol. It

also shows a wider distribution of recovery time in the TCIA sevoflurane group than the TCI propofol group. It can be concluded that there was a statistically significant difference in recovery time between the two groups (p<0.05).

The total average use of TCIA sevoflurane per anesthetic duration was as much as 0.12 ml/min (7.2 ml/hour). While the TCI propofol average use per anesthetic duration was 7.25 mg/min (435.0 mg/hour). The sevoflurane unit price in Sanglah General Hospital pharmacy in December 2015 was IDR (Indonesian Rupiah) 1,465,000 per 250 ml bottle, while the propofol price was IDR20,782 per 200 mg ampoule. This means, the sevoflurane price was IDR5,860/ml and the propofol IDR103.91/mg.

Propofol as an intravenous drug could not simply be calculated per ml usage, but it is counted by the number of the opened ampoules. However, the cost minimization analysis between the two groups has no significant difference. The price of the hypnotic drug cost for induction and maintenance in TCIA sevoflurane group was IDR152,360 (IQR 70,320), while in the TCI propofol the price was IDR187,038 (IQR 41,564). Based on the Mann-Whitney U test, the cost minimization analysis from the two groups has no significant difference (p=0.146). Table 3 shows the hypnotic drug cost per

minute was IDR598.43 (IQR 112.47) in the TCIA sevoflurane group, while the TCI propofol group was IDR703.27 (IQR 156.73). However, the statistical analysis shows no significant difference between the two groups ( $p=0,138$ ).

In emodynamic parameters, based on the mean arterial pressure which was depicted on TAR1 (baseline mean arterial pressure), the obtained mean difference is 2.7 (1.4-6.8, 95%CI). The mean difference of the post induction mean arterial pressure (TAR2) is 2.6 (-3.0-8.2, 95%CI). The mean difference of the post intubation mean arterial pressure is 2.9 (-6.0-5.2, 95%CI). The result indicates that in the population, the TAR clinical value did not differ between those two groups at a 95% confidence interval. The heart rate variable consists of N1 as the baseline heart rate, and N2 as the post induction heart rate, and N3 as the post intubation heart rate. The mean difference of the N1 is 2.3 (-3.1-7.7, 95%CI).

The mean difference of the N2 is -1.1 (-6-3.9, 95%CI). The mean difference of the N3 is -1.9 (-7.4 -3.6, 95%CI). They indicate that in the population, the heart rate clinical value did not differ between the two treatment groups at 95% confidence interval.

In the other hand, the mean difference of the recovery time is 3.5 (1.9-5.1, 95%CI). This result suggests that in the population, the TCIA sevoflurane patient recovers faster rather than the TCI propofol patients at 95% confidence interval. In the cost comparison of the hypnotic drug between the two groups, the mean difference is IDR17,399.9 (IDR8,457-IDR43,257, 95%CI). The result indicates that TCIA sevoflurane is cheaper than the TCI propofol.

## DISCUSSION

The total amount of sevoflurane and propofol per duration of surgery was found different in both groups, due to the different main drug in anesthetic management. A previous research by Iswahyudi, et al. found that in a group treated with sevoflurane, the surgery lasted for 161.33 minutes ( $\pm 28.99$ ), and the ratio of sevoflurane per time unit was 0.49 ml/min ( $\pm 0.077$ ).<sup>12</sup> In this study, a BIS monitor was used to facilitate the depth of anesthesia continuously, whereas Iswahyudi et al used the index of consciousness (IOC).<sup>12-14</sup> An end tidal was used in our study, with a low flow control inhaled agent and technique in applied anesthesia machine. It would vary the amount of the volatile anesthetic agents given and inspired, depends on the fresh gas flow. Our study shows the ratio of drug needed is 75.51% per unit time. However, literatures stated that a bispectral index monitor

(BIS index) could reduce the dose of anesthetic drug usage by up to 30%.<sup>13-14</sup>

In this study, the recovery time in the TCIA sevoflurane group was 8 minutes (IQR 3), whereas in the TCI propofol group was 11.5 minutes (IQR 3). Despite the difference in the median recovery time, this distinction might not have a clinical effect in ASA physical status I and II patients. But, in patients with a higher physical status ASA, it would shorten the recovery time, shorten the evaluation of patients, and reduce the morbidity and the cost of care reduction.<sup>1-7</sup>

The cost minimization analysis between two groups shows no significant difference. The hypnotic drug cost in the TCIA sevoflurane group was IDR152,360 (IQR 70,320) and in the TCI propofol was IDR187,038 (IQR 41,564). The Mann-Whitney U test shows no significant difference between the two anesthetic cost ( $p=0.146$ ). The cost per minute of the hypnotic drug in the TCIA sevoflurane group was IDR598.43 (IQR 112.47), whereas in the TCI propofol group was IDR703.27 (IQR 156.73). The Mann-Whitney U test also shows no significant difference ( $p=0.138$ ).

Furthermore, at 95%CI, the clinical values of other variables such as TAR (mean arterial pressure) and N (heart rate) show no difference. But, the TCIA sevoflurane group recovers faster than the TCI propofol group at 95%CI. In addition, the cost comparison of the hypnotic drug at 95%CI shows that TCIA sevoflurane is IDR17,399.9 cheaper than the TCI propofol. Based on these two findings of the recovery time and the cost difference, we recommend the use of TCIA sevoflurane over TCI propofol.

The cost analysis above did not include the costs of N<sub>2</sub>O and O<sub>2</sub>, a muscle relaxant, opioid drugs, a disposable equipment such as a nasal cannula, an orotracheal tube, an infusion set, an intravenous catheter, and gloves. The charges for running the anesthetic and the monitoring tools were not included in the calculation. And, the salaries and the wages for staff, which is the biggest cost of hospital services, were also not included in this study. We did this to know the cost of sevoflurane and propofol used for hypnotic drug in general anesthesia solely and to minimize the bias from other components.

A hypotensive incident post-induction in the TCIA sevoflurane group was 20.0%, whereas in the TCI propofol group was 16.75%. But, the Pearson chi-square test finds no significant difference ( $p=0.739$ ). The incidence of hypotension is influenced by the patient's general condition and the effect of the anesthetics during the induction phase. The general state of the patient is a state of hypovolemia before induction and the presence of other

comorbidities.<sup>8</sup> In this study, the factors beyond anesthesia techniques that influence the incidence of hypotension have been eliminated by patient exclusion. Therefore, the anesthetic technique is the only factor affecting the incidence of hypotension.

## CONCLUSION

There was no significant statistical difference between the cost of the target controlled inhalational anesthesia using sevoflurane with a low fresh gas flow 2 liter per minute compared to the target controlled infusion using propofol in physical status ASA I-II patients who underwent a major oncologic surgery in Sanglah General Hospital, Denpasar, Bali, Indonesia. In contrast, based on the clinical values, the TCIA sevoflurane group recovers faster than the TCI propofol group at 95% CI. In addition, the cost comparison of the hypnotic drug at 95%CI shows that the TCIA sevoflurane is cheaper than the TCI propofol for a major oncologic surgery with a long duration.

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