

Comparison of the Effectiveness of the Eleveld and Schnider Target-Controlled Infusion (TCI) Methods in Achieving Depth of Anesthesia

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Abstract

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Background: Target-controlled infusion (TCI) of propofol is an anesthetic method that enables precise drug administration based on pharmacokinetic models. Schnider and Eleveld are two TCI propofol models that differ in predicting effect-site concentrations in the brain and responses measured by the Bispectral Index (BIS). This study aims to compare the effectiveness of both models in achieving optimal anesthesia depth and evaluate associated hypotension as a side effect.

Methods: This double-blind, parallel randomized controlled trial involved 44 patients aged 18–64 years undergoing elective surgery under general anesthesia. Patients were randomly assigned to two groups: the TCI Eleveld group (n = 22) and the TCI Schnider group (n = 22). The primary outcomes measured were CeP50 (effect-site concentration required to achieve BIS 50), total propofol dosage, and the incidence of hypotension.

Result: The TCI Eleveld group required a lower propofol concentration than the TCI Schnider group (3.05 mcg/mL vs. 3.8 mcg/mL; $p < 0.001$). The average propofol consumption was also lower in the Eleveld group (7.44 mg/kg/h vs. 8.19 mg/kg/h; $p = 0.001$). The incidence of hypotension showed no significant difference between the two groups (27.3% vs. 36.4%; $p = 0.517$).

Conclusions: The Eleveld TCI model is more effective than the Schnider model in optimizing anesthetic depth with a lower propofol dose. The reduced propofol usage in the Eleveld model potentially lowers the risk of hypotension, making it a better choice for general anesthesia.

Introduction

Maintaining an optimal depth of anesthesia is a fundamental goal in perioperative care to ensure patient safety, prevent intraoperative awareness, and

minimize adverse physiological responses.¹ Inadequate anesthesia can lead to sympathetic nervous system activation—manifested as hypertension, tachycardia, and movement—which increases surgical risk and patient

discomfort. Conversely, excessive anesthetic depth may cause profound hypotension and reduced cerebral perfusion, contributing to postoperative complications such as delayed emergence and cognitive dysfunction.² Studies have shown that maintaining a bispectral index (BIS) value between 40 and 60 correlates with a lower incidence of awareness and better overall anesthetic control.^{2,3} To manage this balance effectively, modern anesthetic practice increasingly utilizes target-controlled infusion (TCI) systems, which deliver drugs like propofol based on pharmacokinetic (PK) and pharmacodynamic (PD) models that estimate drug concentration at the effect site—the brain.

The Schnider TCI model has been widely adopted for propofol administration in adults due to its simplicity and proven efficacy.⁴ It employs a three-compartment PK model and accounts for covariates such as age, lean body mass, and height to calculate plasma and effect-site concentrations. Its fixed effect-site equilibration constant (ke_0) reflects a standardized delay between plasma and brain concentration, assuming homogeneity across adults.⁴ While the model performs well in routine cases, it lacks adaptability for special populations like the obese, elderly, or pediatric patients, whose physiological parameters significantly influence drug distribution and sensitivity. For instance, aging alters hepatic metabolism and reduces central nervous system responsiveness, affecting both drug clearance and depth of sedation.

The Eleveld TCI model, on the other hand, introduces a more sophisticated approach, built from a large dataset encompassing a broader demographic—including neonates, children, adults, and elderly individuals.⁵ It incorporates dynamic covariate scaling to account for physiological differences in body composition, age-dependent metabolic rates, and sex-related variations. Importantly, it uses a population-based Bayesian framework and incorporates a variable ke_0 , which allows for more accurate predictions of the delay between

plasma concentration and effect-site concentration.⁵ This physiologically informed modeling aims to improve the precision of propofol delivery and reduce the duration and frequency of deviations from the target BIS range. Early studies suggest that the Eleveld model results in more stable hemodynamics and faster attainment of target sedation levels across patient groups.^{4,6,7}

Despite the theoretical advantages of the Eleveld model, direct comparative studies evaluating its clinical performance against the Schnider model are still scarce. Determining which model better maintains target anesthetic depth—especially in patients with varied physiological profiles—is crucial for improving safety, efficiency, and patient outcomes in modern anesthetic practice. This study aims to fill that gap by comparing the effectiveness of the Eleveld and Schnider TCI models in achieving and maintaining BIS values within the optimal range during general anesthesia, thereby providing evidence-based insights for TCI model selection in diverse clinical settings.

Material And Methods

This randomized controlled trial (RCT) was conducted in March 2025 at Rumah Sakit Umum Pusat Prof. Dr. I.G.N.G. Ngoerah, Denpasar, Bali, Indonesia, with ethical approval from the institutional review board (Registration No. 0632/UN14.2.2.VII.14/LT/2025). The study adhered to the Consolidated Standards of Reporting Trials (CONSORT) guidelines to ensure methodological rigor and transparency.⁸ Data analysis followed the intention-to-treat principle, and patient confidentiality was maintained throughout.

Eligible participants were adults aged 18 to 64 years, classified as American Society of Anesthesiologists (ASA) physical status I or II, and scheduled for surgery under general anesthesia. Patients were excluded if they had uncontrolled systemic illnesses (e.g., hypertension, diabetes, hyperthyroidism, or pheochromocytoma), severe neurological disorders, known allergies to propofol, a body mass index (BMI) over 25 kg/m², a history of alcohol use, or

psychiatric medication use (e.g., benzodiazepines). Participants requiring additional sedatives to achieve a BIS value of 50 or those with persistent hypotension needing continuous vasopressors were considered dropouts.

Participants were randomly assigned using block randomization via sealed envelopes, with the sequence generated from <http://randomizer.org/>. Randomization was concealed until immediately before anesthesia induction. The two intervention arms involved TCI of propofol using either the Eleveld or Schnider pharmacokinetic model. In the Eleveld group, TCI was administered using a device programmed with the Eleveld model, while the Schnider group received TCI with the Schnider model on the same system.

The study evaluated three primary clinical outcomes: (1) the effect-site concentration (Ce) of propofol required to achieve optimal anesthesia depth, defined by a BIS of 50; (2) average intraoperative propofol consumption; and (3) the incidence of hypotension, defined as a systolic blood pressure below 90 mmHg. All intraoperative parameters and events were recorded by blinded investigators.

Operational definitions were standardized. The Ce represents the estimated concentration of propofol at the brain (target organ), displayed by the TCI machine in micrograms per milliliter ($\mu\text{g/mL}$). Optimal anesthetic depth was indicated by a BIS value of 50, a numerical EEG-based index ranging from 0 to 100 used to assess consciousness. Average propofol consumption was calculated from induction to the cessation of TCI, expressed in mg/kg/h . Induction was defined as the period from the start of propofol administration to successful endotracheal intubation. Age was verified via medical records and ID; blood pressure was measured noninvasively during surgery (systolic and diastolic, in mmHg); and BMI was calculated in kg/m^2 . Hypotension was defined as systolic blood pressure <90 mmHg. ASA physical status was categorized according to the American Society of Anesthesiologists

classification, with only ASA I–II patients included.

Procedural Protocol for the TCI Propofol Eleveld Group

Patients in the TCI Propofol Eleveld group received standard operating room monitoring, including ECG, non-invasive blood pressure, and pulse oximetry. While supine, their forehead was cleansed and dried before a BIS Quatro sensor was applied and connected to a BIS monitor to establish baseline BIS readings. The TCI device was programmed with the Eleveld pharmacokinetic model using patient-specific data (age, sex, height, weight, and opioid use). A 50 mL syringe containing propofol (10 mg/mL) was loaded into the pump and connected via a 150 cm extension line. Anesthetic induction began at a Ce of 1 mcg/mL and was titrated in 0.5 mcg/mL increments, with BIS monitoring to guide sedation. Once a BIS of 50 was achieved, Ce, blood pressure, and MAP were recorded. Fentanyl (2 mcg/kg) and atracurium (0.5 mg/kg) were administered to provide analgesia and facilitate intubation. After intubation, Ce was adjusted to maintain a BIS value of approximately 50, with continued documentation of anesthetic and hemodynamic parameters. During maintenance, propofol Ce was titrated by ± 0.5 mcg/mL as needed, along with fentanyl (0.5–1 mcg/kg) and atracurium (0.1 mg/kg) for muscle relaxation. Hypotension, defined as a systolic BP <90 mmHg, was managed initially with a crystalloid fluid bolus, followed by ephedrine 5–10 mg IV if needed. All hypotensive episodes were recorded. Patients requiring continuous vasopressors or additional sedatives to achieve BIS 50 were classified as dropouts. At the end of surgery, operative duration and total propofol usage were recorded for further analysis.

Procedural Protocol for the TCI Propofol Schnider Group

Patients assigned to the TCI Propofol Model Schnider gPatients in the TCI Propofol Schnider group received standard intraoperative monitoring, including ECG, non-invasive blood pressure, and pulse oximetry upon

entering the operating room. While in the supine position, their forehead was cleaned and dried before applying a BIS Quatro sensor, which was connected to a BIS monitor to obtain baseline readings. The TCI device was then set to the Schnider pharmacokinetic model using patient-specific inputs (age, sex, height, and weight). A 50 mL syringe containing propofol (10 mg/mL) was loaded into the pump and connected via a 150 cm extension tube. Anesthetic induction began at an Ce of 1 mcg/mL, titrated in 0.5 mcg/mL increments until a BIS value of 50 was achieved. At this point, Ce, blood pressure, and MAP were documented. Fentanyl (2 mcg/kg) and atracurium (0.5 mg/kg) were administered to provide analgesia and muscle relaxation for intubation. Post-intubation, Ce was adjusted to maintain a BIS of 50, with continued monitoring of hemodynamic parameters. During maintenance, propofol Ce was titrated by ± 0.5 mcg/mL, with additional fentanyl (0.5–1 mcg/kg) and atracurium (0.1 mg/kg) boluses as needed. Hypotension (systolic BP <90 mmHg) was initially managed with a crystalloid bolus (10 mL/kg); if unresolved, ephedrine (5 mg IV) was given and repeated every 5 minutes. Persistent hypotension required vasopressor support. All hypotensive episodes were recorded, and patients needing continuous vasopressors or additional sedatives to maintain BIS 50 were classified as dropouts. At the end of surgery, total operative time and propofol consumption were documented for analysis. Upon receiving standard monitoring upon entering the operating room, including the placement of ECG electrodes, a blood pressure cuff, and pulse oximetry for continuous peripheral oxygen saturation monitoring. In the supine position, the patient's forehead was cleaned with soap to remove oil and debris, then dried. A BIS Quatro electrode was applied to one side of the forehead, connected to the BIS monitor, and calibrated to record the patient's baseline BIS value. The TCI machine was programmed using the Schnider pharmacokinetic model with patient-specific data including age, sex,

height, and weight. Propofol 10 mg/mL was loaded into a 50 mL syringe, inserted into the TCI pump, and connected to the patient via a 150 cm extension tube. Anesthetic induction began with a Ce of 1 mcg/mL, with BIS monitoring to assess sedation depth. Ce was titrated upward in increments of 0.5 mcg/mL after stabilization at each level until a BIS value of 50 was reached, at which point Ce, blood pressure, and MAP were recorded. Fentanyl 2 mcg/kg and atracurium 0.5 mg/kg were then administered for analgesia and neuromuscular blockade to facilitate intubation. Following intubation, propofol Ce was titrated to maintain a BIS of 50, with continued documentation of Ce, blood pressure, and MAP. Maintenance anesthesia involved titration of propofol Ce by ± 0.5 mcg/mL, fentanyl at 0.5–1 mcg/kg, and atracurium 0.1 mg/kg boluses for muscle relaxation. Hypotension, defined as a systolic blood pressure <90 mmHg, was managed initially with a 10 mL/kg crystalloid fluid bolus. If unresponsive, ephedrine 5 mg IV was administered and repeated every 5 minutes as needed. Persistent hypotension was treated with vasopressor titration to maintain systolic BP above 90 mmHg, with all hypotensive episodes recorded. Patients requiring continuous vasopressors or additional sedatives to achieve BIS 50 were categorized as dropouts. At the end of surgery, both the total operative duration and cumulative propofol use were recorded for analysis.

Statistical Analysis

All statistical analyses were performed using SPSS version 26. Descriptive statistics were used to summarize the baseline characteristics of participants and study variables. Continuous variables such as age, weight, height, BMI, Ce, BIS-50 time, and total propofol consumption were expressed as mean $\pm$ standard deviation (SD), as the data were normally distributed. Categorical variables such as sex, ASA status, and incidence of hypotension were presented as frequencies and percentages.

To compare means between the two independent groups (Elefeld vs. Schnider), an Independent Samples T-test

was used. Homogeneity of variance was assessed using Levene's Test. A Chi-Square test was employed to compare categorical variables. If the assumptions for the Chi-Square test were not met, Fisher's Exact Test was used as an alternative. All tests were two-tailed, and a p-value < 0.05 was considered statistically significant.

Result

A total of 44 participants were assessed for eligibility in this study, with

none excluded for not meeting the inclusion criteria, declining to participate, or other reasons. All eligible participants (n = 44) were randomized into two groups: Group P1 (TCI Eleveld, n = 22) and Group P2 (TCI Schnider, n = 22). All participants received the allocated intervention, and there were no dropouts during follow-up. Consequently, all 44 participants completed the study and were included in the final analysis, with no exclusions from either group (Figure 1).

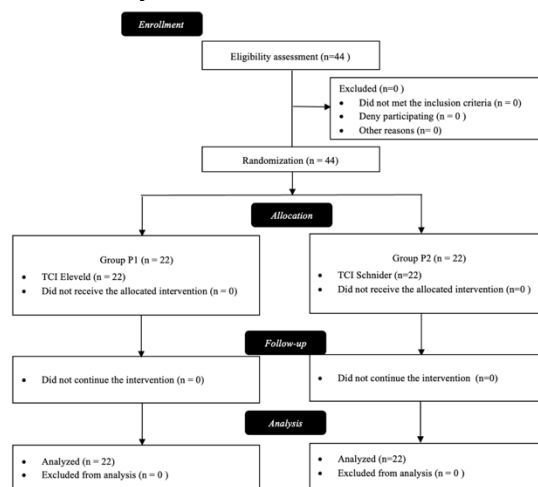


Figure 1. CONSORT flow diagram

A total of 44 subjects were randomly assigned into two groups: the TCI Eleveld group (n = 22) and the TCI Schnider group (n = 22). Demographic data showed no significant differences between the groups. The mean age was 38.77 vs. 40.36 years (p = 0.729), mean body weight was 58.5 vs. 60.41 kg (p = 0.568), mean height was 159.55 vs. 161.87 cm (p = 0.417), and mean BMI was 22.82 vs. 22.99 (p = 0.843). There was also no significant difference in sex distribution, with more females than males in both groups (p = 0.112), nor in ASA physical status, with equal numbers of ASA I and II subjects in both groups (p = 1.000). The types of surgeries performed did not differ

significantly between groups, with nasal procedures (FESS, rhinotomy, and conchotomy) being the most common (p = 0.649). Categorical variables were assessed for normality using cross-tabulation and the Chi-Square test (as expected values were >5), yielding p > 0.05, indicating normal distribution. Normality for numerical variables was assessed using the Shapiro-Wilk test, which also showed p > 0.05, indicating normal distribution and allowing for the use of independent t-tests. For variables that did not follow a normal distribution, the Mann-Whitney U test was applied to determine any significant differences between the two groups.

Table 1. Characteristics of Study Participants

Variable	TCI Eleveld (n = 22)	TCI Schnider (n = 22)	p-value
Age (years)	38.77 ± 14.82	40.36 ± 15.47	0.729*
Body Weight (kg)	58.5 ± 11.42	60.41 ± 10.55	0.568*
Height (cm)	159.55 ± 8.25	161.87 ± 10.39	0.417*
Body Mass Index (kg/m ²)	22.82 ± 3.26	22.99 ± 2.12	0.843*
Sex			0.112†

- Male	5 (22.7%)	10 (45.5%)	
- Female	17 (77.3%)	12 (54.5%)	
Type of Surgery			0.649*
- Tympanoplasty	8 (36.4%)	7 (31.8%)	
- Mastectomy	2 (9.1%)	5 (22.7%)	
- Nasal Surgery	9 (40.9%)	7 (31.8%)	
- Total Thyroidectomy	3 (13.6%)	3 (13.6%)	
ASA Classification			1.000†
- ASA I	11 (50.0%)	11 (50.0%)	
- ASA II	11 (50.0%)	11 (50.0%)	

Note: Data with normal distribution are presented as mean $\pm$ standard deviation; non-normally distributed data are presented as median (interquartile range). Normality was tested using the Shapiro-Wilk test ($n < 50$).

*Independent T-test, †Chi-square test, *Likelihood Ratio (LR) test. A p-value > 0.05 indicates no significant difference between the groups.

Table 2 presents the intraoperative outcome variables comparing the TCI Eleveld and TCI Schnider groups. The median time to reach BIS 50 was 8.0 (IQR 3.0) minutes in the Eleveld group and 8.0 (IQR 5.38) minutes in the Schnider group ($p = 0.342$). The median CeP50 was 3.05 (IQR 0.62) $\mu\text{g/mL}$ in the Eleveld group and 3.8 (IQR 0.72) $\mu\text{g/mL}$ in the Schnider group ($p < 0.001$). The total propofol dose was 1025 (IQR 916.25) mg in the Eleveld group and 1365 (IQR 877.50) mg in the Schnider group ($p = 0.166$). The average propofol dose was 7.44 (IQR 0.80) mg/kg/h in the Eleveld group and 8.19 (IQR 1.81) mg/kg/h in the Schnider group ($p = 0.001$). The incidence of hypotension was reported in 6 (27.3%) participants in the Eleveld group and 8 (36.4%) in the Schnider group, while 16 (72.7%) and 14 (63.6%) participants in each group, respectively, did not experience hypotension ($p = 0.517$).

Schnider group ($p = 0.166$). The average propofol dose was 7.44 (IQR 0.80) mg/kg/h in the Eleveld group and 8.19 (IQR 1.81) mg/kg/h in the Schnider group ($p = 0.001$). The incidence of hypotension was reported in 6 (27.3%) participants in the Eleveld group and 8 (36.4%) in the Schnider group, while 16 (72.7%) and 14 (63.6%) participants in each group, respectively, did not experience hypotension ($p = 0.517$).

Variable	TCI Eleveld (n = 22) Median (IQR)	TCI Schnider (n = 22) Median (IQR)	p-value
Time to Reach BIS 50 (minutes)	8.0 (3.0)	8.0 (5.38)	0.342*
CeP50 ($\mu\text{g/mL}$)	3.05 (0.62)	3.8 (0.72)	$<0.001^*$
Total Propofol Dose (mg)	1025 (916.25)	1365 (877.50)	0.166*
Average Propofol Dose (mg/kg/h)	7.44 (0.80)	8.19 (1.81)	0.001*
Hypotension			0.517*
- Yes	6 (27.3%)	8 (36.4%)	
- No	16 (72.7%)	14 (63.6%)	

Note: Data were not normally distributed based on the Shapiro-Wilk test ($p < 0.05$) and are therefore reported as median (interquartile range).

*Statistical analysis was performed using the Mann-Whitney U test; p-values < 0.05 were considered statistically significant.

Discussion

This study compared the effectiveness of the Eleveld and Schnider TCI models for propofol administration in achieving and maintaining anesthetic depth, focusing on Ce, total propofol consumption, and hypotension incidence. The results demonstrated a significantly lower CeP50 in the Eleveld group (3.05 $\mu\text{g/mL}$) compared to the Schnider group (3.8 $\mu\text{g/mL}$, $p < 0.001$), indicating that the Eleveld model required a lower propofol concentration to achieve a BIS value of 50. This finding aligns with previous

studies suggesting that the Eleveld model provides a more accurate pharmacokinetic representation across diverse populations, including younger, older, and obese patients.^{5,9} Studies by Eleveld et al. (2018) and Absalom et al. (2021) have shown that the Eleveld model's dynamic adjustments for age, sex, and weight improve dosing precision compared to older models like Schnider, which was developed using a more limited patient dataset.^{5,9}

The rationale for this study was based on the differences in PK and PD modeling

between Eleveld and Schnider. The Schnider model, developed primarily for lean adults, fixes the ke_0 (effect-site equilibration rate constant), which may lead to overestimation of C_e in heavier or elderly patients.⁴ Conversely, the Eleveld model incorporates variable ke_0 adjustments and a broader dataset, making it more adaptable to different patient demographics. This adaptability likely contributed to the lower total propofol consumption observed in the Eleveld group, though this difference was not statistically significant ($p = 0.166$).¹⁰ The ability to achieve anesthetic depth at a lower C_e suggests that the Eleveld model optimizes drug delivery while minimizing exposure, which is particularly relevant for patients at risk of drug accumulation, such as those with reduced hepatic metabolism.^{10,11}

From a physiological perspective, the differences in propofol dosing and C_e between the models can be explained by variations in brain sensitivity, volume of distribution, and clearance mechanisms.¹² The CNS sensitivity to propofol varies with age and weight, factors that are better accounted for in the Eleveld model. Propofol undergoes extensive hepatic metabolism, and its distribution is influenced by cardiac output and protein binding.^{12,13} The Schnider model's reliance on lean body mass calculations may underestimate distribution in certain patients, leading to a higher C_e requirement to maintain BIS at 50.⁴ The Eleveld model's incorporation of weight-based allometric scaling likely results in a more physiologically accurate prediction of effect-site concentration, reducing interpatient variability in response.¹⁴

Hypotension, a common concern with propofol-based anesthesia, was observed in 6 patients (27.3%) in the Eleveld group and 8 patients (36.4%) in the Schnider group, with no significant difference ($p = 0.517$). This suggests that while C_e requirements differed, the overall hemodynamic impact of propofol was similar between the two models. Prior research has established that propofol-induced vasodilation is dose-dependent and influenced by total drug exposure

rather than peak concentration alone.^{15,16}

The fact that total propofol consumption was not significantly different between the two groups may explain why hypotension rates remained comparable. Future studies should explore whether individualized C_e targeting, guided by real-time hemodynamic parameters, could further optimize TCI-based anesthesia and reduce hypotensive events.

This study had several limitations. First, the sample size was relatively small ($n = 44$), which may limit the statistical power and the generalizability of the findings to broader patient populations. Second, the study focused primarily on intraoperative anesthetic parameters and did not evaluate important postoperative outcomes such as recovery time, emergence quality, or other potential side effects of propofol administration (e.g., nausea, cognitive dysfunction). Lastly, this was a single-center study conducted in a specific clinical setting, which may restrict the external validity of the results. Future multicenter trials with larger sample sizes and comprehensive perioperative outcome evaluations are recommended to validate and expand upon these findings.

Conclusion

The Eleveld TCI Propofol model demonstrated superior performance compared to the Schnider model in achieving optimal anesthetic depth with a lower average dose of propofol, indicating better pharmacokinetic efficiency. Although the difference was not statistically significant, the incidence of hypotension was lower in the Eleveld group, suggesting a potentially safer hemodynamic profile. These findings support the Eleveld model as a more favorable option for general anesthesia, particularly in patients with higher cardiovascular risk. Further research is recommended to assess recovery times and postoperative side effects associated with both models.

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