



Estimation of the Median Effective Dose of Propofol for Colonoscope Advancement to the Rectosigmoid Junction in Geriatric Patients: A Prospective Dose-finding Study

Geriatric Hastalarda Kolonoskopun Rektosigmoid Bileşkeye İlerletilmesini Sağlayan Propofolün Medyan Etkili Dozunun Tahmini: Prospektif Doz Belirleme Çalışması

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ABSTRACT

Objective: This study aimed to determine the median effective dose (ED₅₀) of propofol monosedation required to achieve well-tolerated and motionless advancement of the colonoscope to the rectosigmoid junction in geriatric patients.

Methods: This prospective dose-finding study was conducted between September 8 and October 8, 2025. Geriatric patients aged ≥65 years with American Society of Anesthesiologists physical status I-III and body mass index <30 kg/m² who underwent elective colonoscopy under propofol monosedation were included. Propofol was administered using a modified Dixon up-and-down method, starting at 1.5 mg/kg with 0.1 mg/kg dose adjustments. Success was defined as colonoscope advancement to the rectosigmoid junction without movement, vocalization, or observable pain-related behavior, together with a Modified Observer's Assessment of Alertness/Sedation score of ≤2 at two minutes after induction. After each success, the next dose was decreased by 0.1 mg/kg; after each failure, it was increased by 0.1 mg/kg.

Results: Eight crossover points were observed, and the study concluded after 29 patients. The ED₅₀ of propofol was 0.57 mg/kg [95% confidence interval (CI), 0.357-0.791], and the ED₉₅ was 1.81 mg/kg (95% CI, 0.094-3.517). Mean total propofol dose was 128.4±47 mg. No clinically significant respiratory

Öz

Amaç: Bu çalışmada, geriatric hastalarda işlemin iyi tolere edilmesini ve kolonoskopun hasta hareketi olmaksızın rektosigmoid bileşkeye ilerletilmesini sağlayan propofol monosedasyonunun medyan etkili dozunun (ED₅₀) belirlenmesi amaçlandı.

Yöntemler: Bu prospektif doz belirleme çalışması 8 Eylül-8 Ekim 2025 tarihleri arasında yürütüldü. Propofol monosedasyonu altında elektif kolonoskopi uygulanan, Amerikan Anesteziyologlar Derneği fiziksel durum sınıfı I-III olan, vücut kitle indeksi <30 kg/m² ve yaşı ≥65 yıl olan geriatric hastalar çalışmaya dahil edildi. Propofol, 1,5 mg/kg başlangıç dozu ve 0,1 mg/kg doz aralıkları kullanılarak modifiye Dixon yukarı-aşağı yöntemiyle uygulandı. Başarı, indüksiyondan iki dakika sonra Modifiye Gözlemcinin Uyanıklık/Sedasyon Değerlendirme Ölçeği skorunun ≤2 olmasıyla birlikte kolonoskopun rektosigmoid bileşkeye hareket, vokalizasyon veya gözlenebilir ağrıyla ilişkili davranış olmaksızın ilerletilmesi olarak tanımlandı. Her başarılı yanıtın sonra bir sonraki hastada doz 0,1 mg/kg azaltıldı; her başarısız yanıtın sonra ise 0,1 mg/kg artırıldı.

Bulgular: Sekiz çapraz geçiş noktası gözlemlendi ve çalışma 29 hasta sonrasında tamamlandı. Propofolün medyan etkili dozu 0,57 mg/kg [%95 güven aralığı (GA), 0,357-0,791], %95 etkili

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Cite this article as: Günel B, Şencan A. Estimation of the median effective dose of propofol for colonoscope advancement to the rectosigmoid junction in geriatric patients: a prospective dose-finding study. Bezmialem Science. 2026;14(4):393-400

Received: 14.07.2026

Accepted: 12.08.2026

Published date: 26.10.2026



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ABSTRACT

depression or airway intervention occurred; median lowest peripheral oxygen saturation (SpO₂) was 97% (91-99). Injection pain occurred in 20.7%, and post-procedural nausea in 3.4% of patients. Heart rate and SpO₂ did not change significantly. Although an overall difference in mean arterial pressure was observed (p=0.030), no significant pairwise differences remained after Bonferroni correction.

Conclusion: The ED₅₀ of propofol for well-tolerated and motionless colonoscopy insertion in geriatric patients was estimated to be 0.57 mg/kg. Given the exploratory nature of this dose-finding study, these findings should be interpreted as preliminary and may contribute to individualized dosing strategies for colonoscopy sedation in this population.

Keywords: Propofol, geriatric, geriatric anesthesia, effective dose, colonoscopy

Öz

dozu ise 1,81 mg/kg (%95 GA, 0,094-3,517) olarak hesaplandı. Ortalama toplam propofol dozu 128,4±47 mg idi. Klinik olarak anlamlı solunum depresyonu veya hava yolu müdahalesi gözlenmedi; en düşük periferik oksijen saturasyonu (SpO₂) medyan değeri %97 (91-99) idi. Enjeksiyon ağrısı hastaların %20,7'sinde, postoperatif bulantı ise %3,4'ünde görüldü. Kalp hızı ve SpO₂ değerlerinde anlamlı değişiklik gözlenmedi. Ortalama arter basıncında genel analizde anlamlı bir farklılık saptanmasına rağmen (p=0,030), Bonferroni düzeltmesi sonrası ikili karşılaştırmaların hiçbirinde anlamlı fark bulunmadı.

Sonuç: Geriatrik hastalarda iyi tolere edilen ve hareketsiz kolonoskop yerleştirilmesi için propofolün ED₅₀ değeri 0,57 mg/kg olarak tahmin edildi. Bu doz belirleme çalışmasının keşifsel niteliği göz önünde bulundurulduğunda, bulgular öncül sonuçlar olarak yorumlanmalıdır. Çalışmanın bulguları bu hasta popülasyonunda kolonoskopi sedasyonu için bireyselleştirilmiş dozlama stratejilerine katkı sağlayabilir.

Anahtar Kelimeler: Propofol, geriatri, geriatrik anestezi, etkili doz, kolonoskopi

Introduction

Propofol is one of the most commonly used agents for sedation during endoscopic procedures (1). It provides rapid emergence, a predictable and consistent depth of sedation, improved patient tolerance, and a complication profile comparable to or better than that of alternative agents (2-5). Propofol may be administered alone or in combination with other sedative agents, with the depth of sedation increasing in a dose-dependent manner (6). Its principal adverse effects include respiratory depression, dose-dependent hypotension, and injection pain, and no specific pharmacological antagonist is available (7,8). Although combination regimens may reduce the propofol dose required and thereby limit dose-dependent adverse effects, they may also delay recovery (6-8).

Age-related pharmacokinetic and pharmacodynamic changes affect the distribution of propofol and the electroencephalographic response to the drug (9). In geriatric patients, lower doses may be sufficient to achieve an equivalent depth of sedation because of age-related reductions in cardiorespiratory, hepatic, and renal function (10).

Nevertheless, evidence regarding the effective dose of propofol monosedation required for successful colonoscopy insertion in geriatric patients remains limited.

Therefore, the present study aimed to determine the median effective dose (ED₅₀) of propofol monosedation required for successful advancement of the colonoscopy to the rectosigmoid junction in adults aged ≥65 years.

Methods**Study Design**

A prospective dose-finding study was conducted using the up-and-down sequential allocation method. Ethical approval for the protocol was granted by the Kocaeli University Clinical Research Ethics Committee (approval no: KAEK/08.bl.02) on April 30, 2025, and the study conformed throughout to Declaration of Helsinki principles. Before the recruitment of participants, the trial was registered on ClinicalTrials.gov on August 25, 2025 (NCT07162805). Participant enrollment and data collection were carried out between September 8 and October 8, 2025. Written informed consent was obtained from every participant only after they had been fully briefed on the study procedures.

Participants

Adults aged ≥65 years, irrespective of sex, who had an American Society of Anesthesiologists (ASA) physical status of I-III and were scheduled to undergo colonoscopy were eligible for participation after providing written informed consent.

Patients were excluded if they declined to take part, had documented hypersensitivity to propofol, soy, peanuts, or egg white, were taking hypnotic, antidepressant, or antipsychotic drugs, or reported habitual alcohol use; had acute or chronic pain; and had either a body weight below 40 kg or a body mass index (BMI) above 30 kg/m²; had previously diagnosed obstructive sleep apnea or a STOP-Bang score of 3 or higher; had a history of anorectal disorders, including hemorrhoids, anal fissure, or anal fistula; had malignancy; had a history of colorectal surgery;

had chronic pulmonary disease or an active respiratory tract infection; had advanced renal or hepatic dysfunction; and had poorly controlled hypertension, defined as systolic blood pressure ≥ 180 mmHg and/or diastolic blood pressure ≥ 110 mmHg.

Randomization and Blinding

Due to the nature of the study, neither randomization nor blinding was performed.

Anesthetic Technique and Dose-finding Methodology

Standard monitoring, including pulse oximetry, electrocardiography, non-invasive blood pressure measurement, and capnography, was applied to every patient upon arrival in the endoscopy unit. Peripheral venous access was secured with a 20- or 22-gauge intravenous cannula, followed by administration of Ringer's lactate solution. Before sedation, patients received oxygen through a nasal cannula at 5 L/min for 3 minutes, and oxygen delivery at the same rate was continued until completion of the procedure. In line with standard clinical practice, colonoscopy was performed with the patient in the left lateral decubitus position. After completion of preoxygenation, intravenous propofol (2,6-diisopropylphenol; propofol 1%, Polifarma® Pharmaceutical Industry, Türkiye) was administered over 20 seconds to induce sedation.

The Dixon up-and-down sequential allocation method was used as the dose-finding strategy in this study (11,12). In this stepwise design, each participant's dose depends directly on how the previous participant responded—an approach long established in clinical pharmacology research (11,12). The starting dose was 1.5 mg/kg, selected with reference to previous endoscopy studies and routine clinical practice. Thereafter, the dose was increased or decreased by 0.1 mg/kg according to the outcome observed in the immediately preceding patient (13,14). Anesthetic management was performed by specialist anesthesiologists (B.G. and A.Ş.). After induction, a 2-minute interval was allowed to achieve maximum drug effect (15). At the beginning of the colonoscopy, the depth of sedation was assessed using the Modified Observer's Assessment of Alertness/Sedation (MOAA/S) scale (16). On this scale, a score of 5 indicates a prompt response to the patient's name spoken normally; 4, a sluggish response to the same stimulus; 3, a response only when the name is called loudly; 2, a response only to gentle-to-moderate physical prompting; and 1, a response elicited only by trapezius squeeze (16).

All procedures were conducted by a specialist endoscopist at the endoscopy unit of University of Health Sciences Türkiye, Kocaeli City Hospital, a tertiary-level referral center. Success was considered achieved when the colonoscope crossed the rectosigmoid junction without movement, vocalization, or observable pain-related behavior, together with a MOAA/S score of ≤ 2 at two minutes after induction.

If these criteria were not met—that is, if movement, vocalization, observable pain-related behavior, or a MOAA/S score of ≥ 3 occurred—the case was considered a failure, and a rescue dose of propofol (0.25-0.5 mg/kg) was titrated and administered. For the subsequent patient, the initial propofol dose was adjusted by 0.1 mg/kg, increased after failure and decreased after success.

Conditions for colonoscope insertion were evaluated only until the instrument had traversed the rectosigmoid junction. After the procedure began, rescue propofol was administered in titrated intravenous doses of 0.25-0.5 mg/kg whenever the patient exhibited observable pain-related behavior, moved, vocalized, or had a MOAA/S score of ≥ 3 . Sedation was subsequently adjusted to maintain a MOAA/S score of ≤ 2 throughout the procedure, with assessments performed at 2-minute intervals. Hemodynamic and respiratory variables, procedural duration, and total drug doses were documented. At the end of the examination, emergence was facilitated using verbal and tactile stimulation. Patients were then transferred to the post-anesthesia care unit and remained under observation until a modified Aldrete score of 10 was reached, after which discharge was permitted.

Primary Outcome

The primary outcome was the determination of the ED₅₀ of propofol required for successful colonoscope advancement to the rectosigmoid junction.

Secondary Outcomes

Secondary outcomes included calculation of the ED₉₅ of propofol required for successful colonoscope advancement to the rectosigmoid junction, the additional and total propofol doses administered, the presence of pain during injection, and the measurement of heart rate (HR), mean arterial pressure (MAP), and peripheral oxygen saturation (SpO₂) at four time points: before sedation (T0), during colonoscope passage through the rectosigmoid junction (T1), two minutes after insertion (T2), and at the end of the procedure (T3). Furthermore, the incidence of hypoxemia (SpO₂ $< 90\%$ for more than 10 seconds), the minimum SpO₂ value observed during the procedure, and procedure interruptions due to airway interventions (chin lift, jaw thrust, mask ventilation) were also evaluated as secondary outcome measures.

Sample Size

In a Dixon up-and-down sequential design study, the non-independence of data and the unknown distribution prevent the establishment of theoretically strict rules for sample size calculation (17). The sample size is determined according to the stop rule (17). Patients should continue to be enrolled until at least six crossover points between effective and ineffective responses are observed (17). Simulation studies have suggested that including 20-40 patients is sufficient to obtain stable estimates of the

target dose for most scenarios (17). Other anesthesia studies using this method have also typically included 20-40 patients (12). In the present study, eight crossover points were considered sufficient for this purpose, and the study was to be terminated once eight crossover points were reached.

Statistical Analysis

Statistical processing was carried out in IBM SPSS Statistics (version 27.0, IBM Corp., Armonk, NY). Normality of continuous variables was assessed using the Shapiro-Wilk test. Normally distributed data were presented as mean ± standard deviation, whereas non-normally distributed data were presented as median with range. Categorical variables were expressed as number and percentage. Temporal changes in hemodynamic and respiratory variables were analyzed using repeated-measures analysis of variance when parametric assumptions were met; otherwise, the Friedman test was used. Bonferroni adjustment was applied for subsequent pairwise comparisons. All tests were two-sided, and p-values <0.05 were considered statistically significant.

Dose-response analyses were performed separately in R software (R Foundation for Statistical Computing, Vienna, Austria). Binary success/failure responses were modeled against the natural logarithm of the initial propofol dose using logistic regression with a logit link (stats::glm, binomial

family). ED₅₀ and ED₉₅ values were obtained by inverse prediction from the fitted model coefficients. Standard errors were estimated using the delta method based on the variance-covariance matrix of the model coefficients, and 95% confidence intervals (CIs) were calculated on the original dose scale using the normal approximation. The fitted logistic regression model was also used to generate the dose-response curve.

Results

Participant Flow and Baseline Data

Recruitment was conducted between September 8 and October 8, 2025. Of the 51 patients assessed for eligibility, 22 did not meet the inclusion criteria, leaving 29 participants for enrollment (Figure 1). The study was terminated after the eighth crossover was reached. No enrolled participants were lost during the study, and all were included in the final analysis. The demographic and clinical characteristics of the study population are shown in Table 1, and the procedural data are presented in Table 2.

Primary Outcome

Analysis performed in R yielded a propofol ED₅₀ of 0.57 mg/kg (95% CI, 0.357-0.791 mg/kg) for successful colonoscope insertion. Responses were evaluated according to the modified Dixon up-and-down design, and the corresponding dose-response findings are presented in Figures 2 and 3.

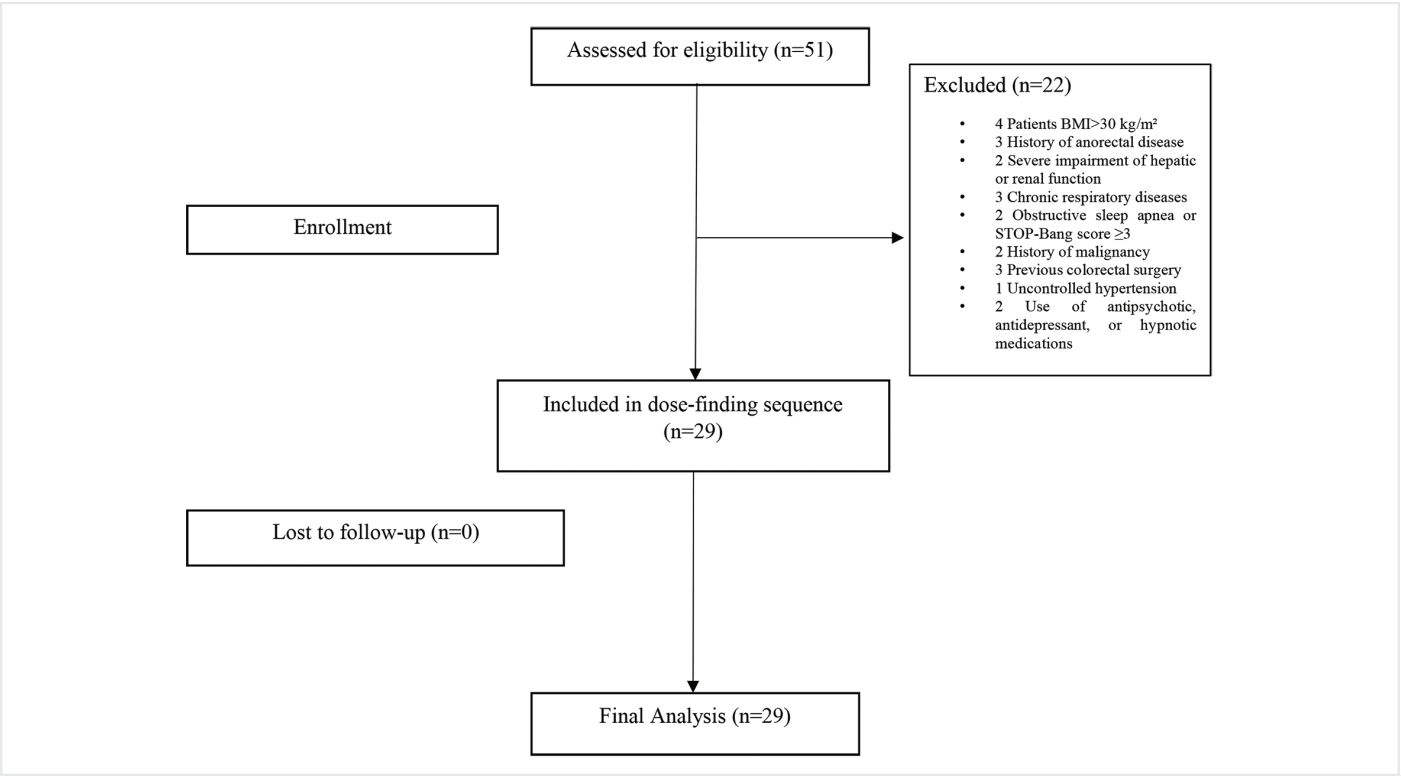


Figure 1. Flow-chart
BMI: Body mass index

Table 1. Patient baseline characteristics

Sex (male/female)	13 (44.8)/16 (55.2)
Age	69 (65-85)
Height (m)	1.7 (1.5-1.8)
Weight (kg)	74±10.1
BMI (kg/m ²)	25.2±3.1
Smoking	4 (13.8)
Hypertension	19 (65.5)
Diabetes mellitus	14 (48.3)
Cardiac disease	9 (31)
Other comorbidities	5 (17.2)
ASA classification II-III	13 (44.8)/16 (55.2)
Mallampati classification I-II	8 (27.6)/21 (72.4)
Indications for colonoscopy	
Surveillance	20 (69)
Suspected tumor	3 (10.3)
Diarrhea	2 (6.9)
Constipation	4 (13.8)
Data are presented as number (%), median (minimum-maximum) or mean ± standard deviation BMI: Body mass index, ASA: American Society of Anesthesiologists	

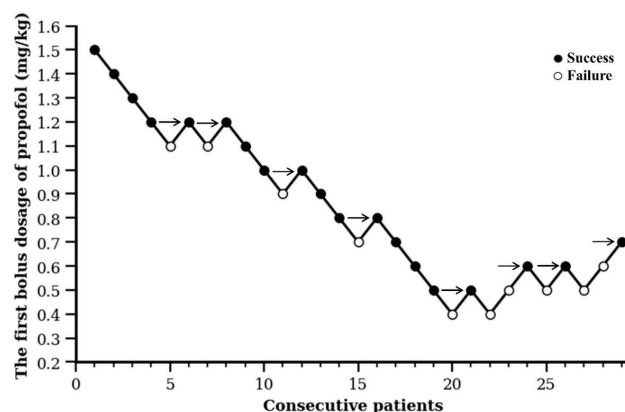
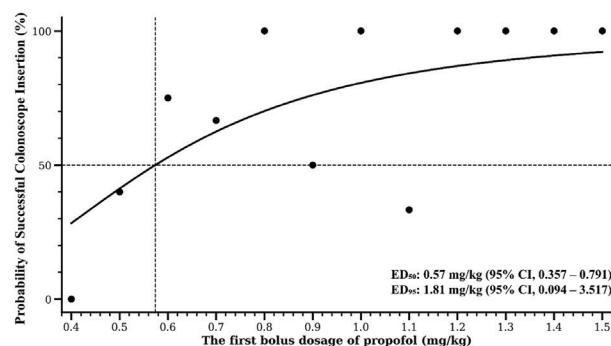
Table 2. Summary of perioperative variables

Initial bolus dose (mg)	61±21.4
Additional propofol dose (mg)	67.5±44.2
Total propofol dose (mg)	128.4±47
MOAA/S at 2 min post-induction (1/2/3/4)	3 (10.3)/21(72.4)/3 (10.3)/2 (6.9)
Procedure duration (min)	10 (4-24)
Lowest SpO ₂ (%)	97 (91-99)
Injection pain	6 (20.7)
Airway intervention	0 (0)
Post-procedural pain	1 (3.4)
Post-procedural nausea	1 (3.4)
Post-procedural vomiting	0 (0)
Data are presented as number (%), median (minimum-maximum) or mean ± standard deviation MOAA/S: Modified Observer's Assessment of Alertness/Sedation, SpO ₂ : Peripheral oxygen saturation	

Secondary Outcomes

Using R software, the ED₉₅ of propofol for successful colonoscope insertion was calculated as 1.81 mg/kg (95% CI, 0.094-3.517). Because this estimate exceeded the observed dose range and had a wide CI, it should be interpreted as an exploratory model-based estimate.

The total propofol dose administered during colonoscopy was 128.4±47 mg, with an additional post-induction dose of 67.5±44.2 mg (Table 2). The median procedure duration was 10 (4-24) min. Pain on injection after induction was

**Figure 2.** Responses of patients with the modified Dixon's up-and-down method**Figure 3.** Dose-response curve

The curve was derived from a logistic regression model relating binary success/failure responses to the natural logarithm of the initial propofol dose

CI: Confidence interval

observed in 6 patients (20.7%). The median of the lowest SpO₂ values recorded during the procedure was 97% (91-99%), and the incidence of airway intervention was 0 (0%). HR and SpO₂ measurements at the four time points did not differ significantly ($p>0.05$). An overall difference was observed in MAP across time points ($p=0.030$); however, none of the pairwise comparisons remained statistically significant after Bonferroni correction (Table 3).

Discussion

This study sought to determine the propofol dose associated with successful colonoscope insertion in geriatric patients with an ASA physical status of I-III and a BMI below 30 kg/m² who received propofol as the sole sedative agent. Based on the modified Dixon up-and-down design, the estimated ED₅₀ was 0.57 mg/kg (95% CI, 0.357-0.791 mg/kg). The

Table 3. Changes in hemodynamic and oxygenation parameters during the procedure

	Before sedation	Endoscope insertion	Two min after endoscope insertion	The end of the procedure	F	p-value
HR (beats/min)	73.3±8.3	72.3±7.5	75.6±9.3	74.7±9.7	2.011	0.160 ^A
MAP (mmHg)	93.2±12.7	86.7±13.4	87.9±14.5	89.1±13	3.648	0.030^{A*}
SpO ₂ (%)	98 (91-100)	98 (92-100)	97 (94-100)	98 (95-100)	-	0.129 ^F

Data are presented as median (minimum-maximum) or mean ± standard deviation

*: p<0.05 was considered statistically significant; since Bonferroni correction was applied in pairwise comparisons, no significant difference was found. ^A: Repeated-measures ANOVA, ^F: Friedman test

HR: Heart rate (beats per minute), MAP: Mean arterial pressure (mmHg), SpO₂: Peripheral oxygen saturation (%), ANOVA: Analysis of variance

corresponding ED₉₅ was estimated as 1.81 mg/kg (95% CI, 0.094-3.517 mg/kg). However, this estimate exceeded the range of doses actually observed in the study and had a wide CI. Therefore, the ED₉₅ should be regarded as a model-based exploratory extrapolation rather than a definitive clinical dosing threshold and requires validation in larger studies.

Rapid onset, short duration of effect, and a favorable recovery trajectory explain why propofol remains a preferred sedative for endoscopic work (1). Previous studies have demonstrated that propofol monotherapy does not present a significant disadvantage compared with combination therapy (4,18). Furthermore, reducing the propofol dose may help minimize clinically relevant dose-related adverse effects, including hypotension, respiratory depression, and excessive sedation (1). Because geriatric patients are more sensitive to propofol's effects on reducing systemic vascular resistance and causing myocardial depression, its use in this population requires special consideration (19). Although adverse effects are a concern in the geriatric population, current evidence suggests that propofol can be used safely at lower doses and with slow administration (4). Another important consideration during colonoscopy is that bowel preparation with sodium phosphate may reduce intravascular volume, thereby increasing the risk of hypotension when combined with sedation (3). Previous studies have investigated the effective dose of propofol in various patient populations (15,20-22). In a comparable study involving non-geriatric adults, Günel and Şencan (22) estimated the propofol ED₅₀ for successful colonoscopy insertion at 1.026 mg/kg (95% CI, 0.735-1.317 mg/kg). Liu et al. (15) reported propofol ED₅₀ and ED₉₅ values of 1.90 and 2.15 mg/kg, respectively, in healthy Chinese adults undergoing upper gastrointestinal endoscopy. In their study, the effective dose was estimated using the modified Dixon up-and-down method, in which each patient's dose was adjusted according to the response of the previous patient (15,21). This method typically requires a minimum of six crossover points to provide reliable results (15). Similar to the study by Liu et al. (15), patient enrollment in our trial was discontinued after eight crossover points were obtained. Another similarity with their study was the use of the MOAA/S score to assess the depth of sedation; in our study, we targeted a MOAA/S score of ≤2 (15). Notably, the ED₅₀ and ED₉₅ values in our

study were markedly lower than those reported by Liu et al. (15), which can largely be attributed to the lower propofol requirements needed to achieve the same depth of sedation in geriatric patients. Hayes et al. (20) also reported an ED₅₀ of 6.1 mg/kg for propofol during deep sedation for gastroduodenoscopy in children. Although this value is considerably higher than that observed in our study, it is not surprising, as children have a larger volume of distribution for propofol, necessitating higher doses to achieve effective sedation (23).

A recent meta-analysis by Ahmer et al. (24) evaluated randomized controlled trials comparing propofol and remimazolam in geriatric patients undergoing gastrointestinal endoscopic procedures and found that propofol was superior in terms of sedation success after the initial dose and time to loss of consciousness. Remimazolam reduced the rates of bradycardia, hypoxemia, and injection pain; however, procedure time, recovery and discharge intervals, respiratory depression, and hypotension were comparable between groups. The authors therefore considered propofol a suitable and effective sedative for geriatric patients (24). Therefore, in order to ensure successful colonoscopy insertion while avoiding excessive sedation, we evaluated the ED₅₀ and ED₉₅ of propofol, still the most commonly used agent for gastrointestinal procedures, in monosedation in the geriatric population. We believe that our findings will contribute valuable data to the literature and inform clinical practice.

By contrast, Borrat et al. (25) reported that 0.75-1 mg/kg of propofol was sufficient for successful upper gastrointestinal endoscopy in patients older than 60 years. Although their patients had demographic characteristics similar to those in our study, the effective dose was slightly higher, possibly because they targeted a MOAA/S score of ≥3 and administered propofol with remifentanyl using target-controlled infusion, whereas we used propofol boluses alone (25). Ethnic differences may also have contributed to the discrepancy in effective dose (15,25).

Injection pain occurred in six patients (20.7%). This rate was lower than that generally reported in the literature (26), but higher than the 11.5% incidence reported by Liu et al. (15). Differences in venous access site, injection rate, and sample size may partly explain the variability among studies.

Study Limitations

Several limitations warrant mention. All enrolled patients were 65 years or older with a BMI under 30 kg/m², and although ASA I-III patients were eligible, the final cohort consisted only of ASA II-III individuals. Therefore, the drug regimen used and the results obtained may not be generalizable to other age groups or different patient populations. Second, sedation depth was assessed solely using the MOAA/S score rather than objective measures such as the bispectral index or electroencephalography. Third, plasma and/or effect-site propofol concentrations were not measured; therefore, a direct dose-exposure-response relationship could not be established, and the findings were based solely on clinical outcomes. Fourth, the limited sample size and exploratory nature of this dose-finding study should be considered when interpreting the dose estimates. In particular, although the modified Dixon up-and-down method is suitable for estimating the ED₅₀, observations tend to cluster around the ED₅₀, limiting the reliability of estimates at the upper end of the dose-response curve, such as the ED₉₀ and ED₉₅. Accordingly, the wide CI of the ED₉₅ estimate in the present study reflects this methodological limitation, and the ED₉₅ should be regarded as exploratory and hypothesis-generating rather than as a definitive clinical dosing recommendation. Fifth, the secondary outcomes evaluated in this cohort should be interpreted cautiously because of the limited sample size. In particular, the absence of clinically significant adverse events or airway interventions should not be regarded as definitive evidence of safety, but rather as an exploratory finding that requires confirmation in larger studies.

Conclusion

Application of the modified Dixon up-and-down approach yielded an estimated propofol ED₅₀ of 0.57 mg/kg (95% CI, 0.357-0.791) for successful passage of the colonoscope through the rectosigmoid junction in geriatric patients. This estimate may serve as an initial reference for tailoring propofol administration during colonoscopy in geriatric patients. However, confirmation in larger and more diverse cohorts is required before a more definitive dosing recommendation can be established.

Ethics

Ethics Committee Approval: Ethical approval for the protocol was granted by the Kocaeli University Clinical Research Ethics Committee (approval no: KAEK/08.bl.02) on April 30, 2025, and the study conformed throughout to Declaration of Helsinki principles.

Informed Consent: Written informed consent was obtained from every participant only after they had been fully briefed on the study procedures.

Declaration on the Use of Artificial Intelligence (AI)

For transparency, the authors note that an artificial intelligence-assisted language model was utilized for text editing and language correction. This assistance was limited to linguistic refinement; all scientific content, critical analysis, and final editorial decisions were made exclusively by the authors.

Footnotes

Authorship Contributions

Surgical and Medical Practices: B.G., A.Ş., Concept: B.G., Design: B.G., Data Collection or Processing: B.G., A.Ş., Analysis or Interpretation: B.G., Literature Search: B.G., A.Ş., Writing: B.G., A.Ş.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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