

# Effect of the infusion rate of propofol on the onset time of rocuronium

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## Abstract

**Background:** Administration of propofol, especially rapid administration, decreases patient cardiac output (CO) to various degrees. CO might influence the buildup of an effective drug level within the neuromuscular junction and affect the onset time of neuromuscular blockers. The present study aimed to investigate the effects of different infusion rates of propofol on patient CO and the onset time of rocuronium.

**Methods:** A total of 90 patients were randomly assigned to receive propofol (2.5 mg/kg) at an infusion rate of 480 mg/min (group A), 240 mg/min (group B), or 120 mg/min (group C). After the administration of propofol, rocuronium (0.6 mg/kg) was administered to facilitate tracheal intubation. The Finometer monitor was used to obtain the cardiovascular profile during the induction of general anesthesia. Neuromuscular relaxation was monitored by acceleromyography using the ulnar nerve at the wrist surface and electrodes with repeated single twitches. Onset time was defined as the time from the beginning of rocuronium injection until 95% twitch depression. The onset time of rocuronium in the three groups was compared using analysis of variance with the post-hoc Tukey test. A *p*-value <0.05 was considered statistically significant.

**Results:** After induction, a significant decrease in CO was observed in group A (21.6% ± 4.6%) when compared with the findings in group B (11.6% ± 4.5%) and group C (9.8% ± 4.6%). The onset time of rocuronium was significantly longer in group A (177.7 ± 17.6 seconds) than in group B (121.3 ± 18.3 seconds) and group C (118.3 ± 12.3 seconds).

**Conclusion:** Rapid administration of propofol significantly delays the onset time of rocuronium by altering CO as measured with the Finometer monitor.

**Keywords:** Cardiac output; General Anesthesia; Neuromuscular blockade; Onset time; Propofol; Rocuronium

## 1. INTRODUCTION

Propofol is a widely used induction agent, and it might cause a significant decrease in blood pressure. The hypotensive effect of propofol is mainly attributed to its marked vasodilator and negative inotropic effects.<sup>1,2</sup> An echocardiographic study of different infusion rates of propofol in low-risk patients indicated that a higher propofol infusion rate might cause a greater decrease in the mean blood pressure by reducing vascular tone (preload and afterload), depressing myocardial contractility, and inhibiting compensatory tachycardia.<sup>3</sup> However, the effect of propofol on cardiac output (CO) remains controversial owing to inconsistent results ranging from no effect<sup>1</sup> to a significant decrease in CO.<sup>4,5</sup> These different findings might be attributed to the various infusion rates of propofol. The peak plasma propofol level is much higher after a rapid induction or bolus dose than after slow injection.

Neuromuscular blockade (NMB) is an adjuvant to general anesthesia and is commonly used to facilitate tracheal intubation

and provide muscle relaxation during surgery. The onset time of NMB is a determining factor for rapidly securing the airway to avoid time delay between anesthesia induction and proper placement of a tracheal tube. Several factors might influence the buildup of a pharmacologically effective drug level within the neuromuscular junction and affect the onset time of NMB, and they include drug potency, administered dose, CO, and regional muscle blood flow.<sup>6</sup>

Rocuronium bromide, a nondepolarizing neuromuscular blocking agent with a rapid onset of action, is indicated in adults and pediatric patients to facilitate both rapid sequence intubation and routine tracheal intubation for general anesthesia. Previous studies have shown that CO is an important factor to determine the onset time of rocuronium. Induction agents that decrease CO might delay the onset of action of rocuronium. On the contrary, agents that increase CO might accelerate the onset of action of rocuronium.<sup>7,8</sup>

Previous studies have investigated the effect of CO on the onset time of rocuronium with administration of ephedrine.<sup>9-12</sup> The present study aimed to investigate the effects of different infusion rates of propofol on the onset time of rocuronium and determine the ideal infusion rate of propofol during the induction of general anesthesia.

## 2. METHODS

After obtaining approval from the institutional review board and informed consent from patients, 90 patients (ASA physical status I-II, age range 20-55 years) who presented for elective surgery under general anesthesia were enrolled into this prospective

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**Table 1**  
Demographic characteristics

Group	A (n = 30)	B (n = 30)	C (n = 30)
Propofol infusion rate, mg/min	480	240	120
Body weight, kg	67 ± 11	65 ± 14	66 ± 12
Age, y	39 ± 12	36 ± 11	38 ± 12
Sex (male/female)	20/10	18/12	18/12
ASA (I/II)	26/4	25/5	26/4

Data are presented as mean ± SD.

randomized study. Patients with a history of body mass index over 30 kg/m<sup>2</sup> and those with evidence of neuromuscular, cardiovascular, hepatic, or renal disease were excluded.

No premedication was administered. Patients were allocated to three groups to receive propofol at an infusion rate of 480 mg/min (group A), 240 mg/min (group B), or 120 mg/min (group C). In the operating room, a 20-gauge intravenous cannula was inserted above the wrist and lactated Ringer's solution was infused at 100 mL/h. Routine monitoring (blood pressure, electrocardiogram, and pulse oximeter) was initiated. Neuromuscular function was monitored with an acceleromyography device (TOF-Watch-SX Acceleromyograph, Organon, Boxtel, The Netherlands) applied to the ulnar nerve. The palm skin temperature of the hand, where neuromuscular functions, was monitored. CO data during the induction of general anesthesia were continuously monitored using Finometer (FMS, Finapres Measurement Systems, Arnhem, The Netherlands), a beat-to-beat finger arterial blood pressure and hemodynamic monitoring system. The Finometer monitor measures hemodynamic parameters, including CO, using noninvasive volume-clamp techniques.

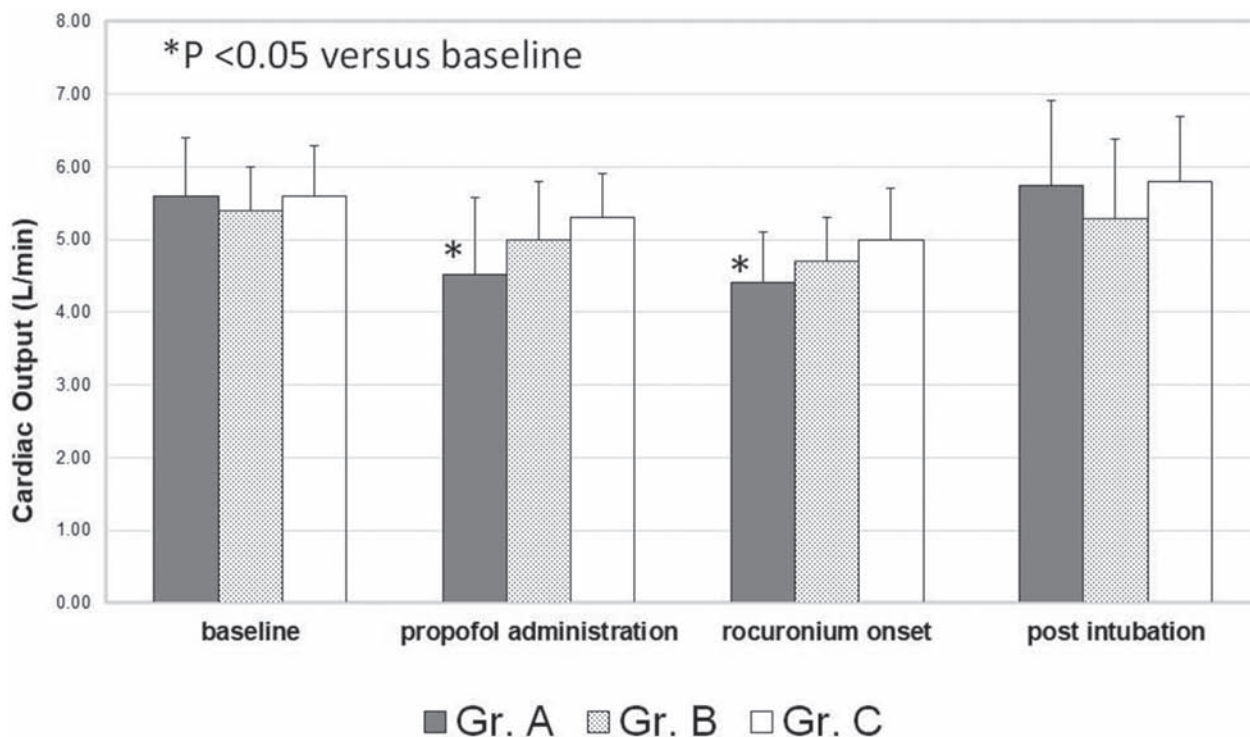
After preoxygenation with 100% oxygen for 3 min, baseline data were collected. Then, propofol (2.5 mg/kg) was administered to induce anesthesia. When the patient lost consciousness

after the propofol administration, the evoked response of the adductor pollicis muscle to ulnar nerve stimulation was initiated, and rocuronium (0.6 mg/kg) was administered. Neuromuscular relaxation was evaluated with repeated single twitches (50 mA, 0.2 ms, 0.1 Hz). Onset time was defined as the time from the beginning of rocuronium injection until 95% twitch depression. Endotracheal tube intubation was performed after 95% twitch depression occurred. The onset time of rocuronium in the three study groups was compared using analysis of variance with the post-hoc Tukey test. Data were recorded at baseline, after induction, and every minute for 5 minutes after intubation. A *p*-value <0.05 was considered statistically significant.

### 3. RESULTS

The study included 90 patients. The demographic characteristics of the patients are presented in Table 1. There were no differences in body weight, age, sex, and ASA status among the three groups. Additionally, there was no difference in the palm skin temperature among the three groups, and the mean temperature was 34.2°C ± 0.87°C. In group A, a significant decrease in CO was observed after the administration of propofol and onset of rocuronium when compared with the value at baseline (*p* < 0.05) (Fig. 1). In group B and group C, there were no significant changes in CO during the induction of general anesthesia. The decrease in CO after the administration of propofol was significantly greater in group A (21.6% ± 4.6%) than in group B (11.6% ± 4.5%) and group C (9.8% ± 4.6%). Additionally, the onset time of rocuronium was significantly longer in group A (177.7 ± 17.6 seconds) than in group B (121.3 ± 18.3 seconds) and group C (118.3 ± 12.3 seconds) (Table 2).

In all groups, there were significant decreases in mean arterial pressure (MAP) after the administration of propofol and onset of rocuronium when compared with the values at baseline (Fig. 2). The mean decrease in MAP after the administration of



**Fig. 1** Change in cardiac output after the induction of general anesthesia and tracheal intubation in the three study groups. \**p* < 0.05 compared with baseline. Data are presented as mean ± SD.

**Table 2**  
Decrease in cardiac output and rocuronium onset time

Group	A (n = 30)	B (n = 30)	C (n = 30)
Propofol infusion rate, mg/min	480	240	120
Onset time, s	177.7 ± 17.6*	121.3 ± 18.3	118.3 ± 12.3
Cardiac output, L/min			
Before	5.6 ± 0.8	5.4 ± 0.6	5.6 ± 0.7
After	4.4 ± 0.7	4.7 ± 0.6	5.0 ± 0.7
Cardiac output decrease, %	21.6 ± 4.6*	11.6 ± 4.5	9.8 ± 4.6

\* $p < 0.05$  compared with other groups. Data are presented as mean ± SD.

propofol was 20% of the baseline value, and there was a further decrease of 26% of the baseline value when the onset time of rocuronium was reached. There was no difference in MAP after intubation when compared with the value at baseline. In all groups, there were no significant differences in heart rate (HR) after the administration of propofol and onset of rocuronium when compared with the values at baseline. In group A and group B, a significant increase in HR was observed after tracheal intubation when compared with the values at baseline (Fig. 3).

#### 4. DISCUSSION

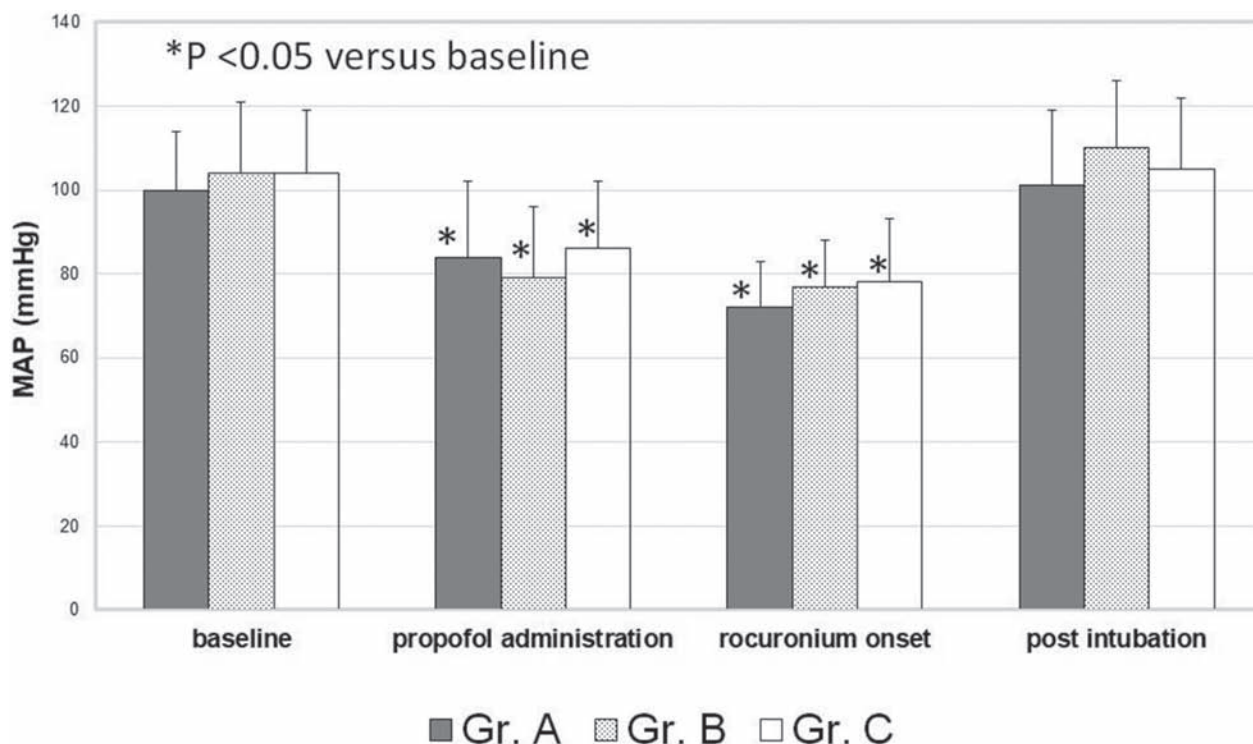
The rapid administration of propofol at an infusion rate of 480 mg/min significantly delayed the onset time of rocuronium (177.7 ± 17.6 seconds) by decreasing CO (21.6% ± 4.6%) as measured using the Finometer monitor. On the contrary, administration at an infusion rate of 240 mg/min or 120 mg/min resulted in a 10% to 12% decrease in CO and did not prolong the onset time. These results indicate that CO is associated with the onset time of rocuronium. Rapid administration of propofol might greatly decrease CO and cause a significant delay in the onset time of rocuronium.

Propofol is a hypnotic agent that is most commonly used for the induction of general anesthesia. As suggested by FDA prescription drug labeling, the typical induction dose of propofol for adult patients aged under 55 years and classified as ASA-PS I or II is 2 to 2.5 mg/kg. Propofol should be titrated at approximately 40 mg every 10 seconds (240 mg/min) until clinical signs indicate the onset of anesthesia. The hemodynamic effects of propofol induction include decreases in arterial blood pressure, systemic vascular resistance, and CO.<sup>3,4,13</sup> The hypotension effect is more significant when propofol is administered as rapid, more frequent, and/or larger boluses. In this study, the infusion rate in group A (480 mg/min) was double the recommended infusion rate.

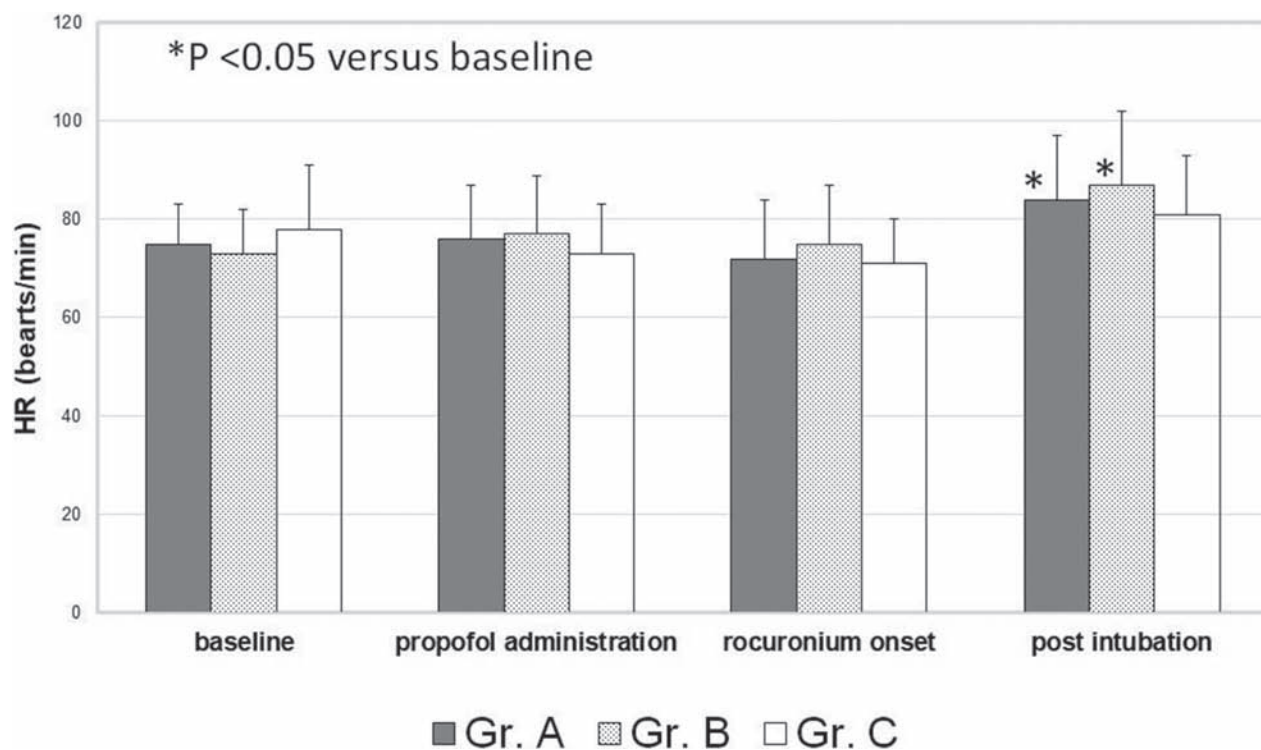
Although several studies have investigated the clinical cardiovascular effects of propofol, it remains uncertain whether propofol decreases CO. Previous studies demonstrated various outcomes ranging from no effect<sup>1,14</sup> to a significant decrease in CO.<sup>4,15,16</sup> However, the differences between studies are difficult to compare owing to varied CO measurement techniques, propofol administration methods, and experimental conditions.

In this study, CO was assessed using the Finometer monitor that provides beat-to-beat measurements using noninvasive volume-clamp techniques. To continuously monitor the change in CO during the induction of general anesthesia, the traditional invasive approach is undesirable. The Finometer monitor allows continuous noninvasive measurements of hemodynamic variables, and previous studies have validated its acceptable performance.<sup>17,18</sup>

Previous studies have shown that ephedrine shortens the onset time of rocuronium by increasing CO and improves the intubation condition.<sup>8,11,12,19,20</sup> Additionally, Han et al demonstrated that ephedrine (70 µg/kg) administered 4 minutes before rocuronium caused the maximum increase in CO. Therefore, the onset time of rocuronium can be accelerated effectively.<sup>9</sup> Moreover, improved intubation conditions and a shortened onset time were demonstrated using a low-dose ketamine with



**Fig. 2** Change in mean arterial pressure after the induction of general anesthesia and tracheal intubation in the three study groups. \* $p < 0.05$  compared with baseline. Data are presented as mean ± SD.



**Fig. 3** Change in heart rate after the induction of general anesthesia and tracheal intubation in the three study groups. \* $p < 0.05$  compared with baseline. Data are presented as mean  $\pm$  SD.

propofol–rocuronium induction.<sup>21</sup> On the contrary, esmolol and a small dose of phenylephrine delayed the onset time of rocuronium after the administration of propofol. It was suggested that esmolol decreases CO and the vasoconstriction effect of phenylephrine prolongs the onset time of rocuronium during the induction of anesthesia using propofol.<sup>11,22</sup>

The effects of propofol on MAP have been studied by Pensado et al, and it was found that the hypotensive effect of a bolus injection of propofol was associated with a direct decrease in systemic vascular resistance.<sup>23</sup> Our results also demonstrated a significant decrease in MAP after propofol injection. With regard to the effect of propofol on HR, there was no significant HR change in our study, and this is because propofol has no clinically significant effect on SA node activity or the intra-atrial conduction system.<sup>24</sup>

In general anesthesia, propofol is commonly used for the induction of anesthesia and rocuronium is used as a NMB agent for endotracheal intubation in hemodynamically stable patients. The goals of smooth induction are to avoid a sudden change in the hemodynamic status and provide a short onset time and good quality of intubation conditions. Although it is recommended to administer propofol at a rate of 40 mg every 10 seconds (240 mg/min), rapid administration of propofol is not unusual in clinical practice. However, the side effects of rapid administration of propofol should be kept in mind by clinicians.

In conclusion, a decrease in CO during the induction of general anesthesia with propofol, especially when rapidly administered, can cause a delay in the onset of a muscle relaxant. The relaxation of airway muscles plays a critical role in airway management during induction. Rapid propofol administration can cause a significant delay in muscle relaxation, which might be dangerous to the patient. Our study findings indicate that an appropriate infusion rate of propofol (ie, <480 mg/min) has a limited effect on CO and thus causes no delay in the onset of a muscle relaxant.

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