

## Dosing study of esmolol for reducing hemodynamic changes during lightwand intubation

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**Background:** Lightwand is a convenient tool that can be used instead of a laryngoscope for intubation. Tracheal intubation causes direct stimulation of the larynx, drastically increasing hemodynamic values including blood pressure and heart rate. This study aims to identify the effect of different doses of esmolol on hemodynamic changes during lightwand intubation.

**Methods:** The study subjects included 140 patients who underwent general anesthesia for elective surgery. The patients were randomly divided into four groups (35 patients in each group). The 'C' group only received 20 ml of normal saline, while the 'E0.5', 'E1', and 'E2' groups received 20 ml of normal saline containing esmolol—0.5 mg/kg, 1 mg/kg, and 2 mg/kg, respectively, injected 2 min prior to intubation. The patients' blood pressure, heart rate, and rate-pressure product were measured six times, before and after the intubation.

**Results:** The degree of heart rate elevation was suppressed in the E1 and E2 groups compared to the C group, and RPP after intubation significantly decreased in the E2 group compared to the C group.

**Conclusions:** Esmolol injection, 1–2 mg/kg, prior to lightwand intubation effectively blunts heart rate elevation, and 2 mg/kg of esmolol injection blunts rate-pressure product elevation.

**Keywords:** Blood pressure; Esmolol; Heart rate; Intubation; Lightwand; Rate pressure product.

## INTRODUCTION

Intubation is a frequent procedure during general anesthesia. However, the traditionally used direct laryngoscope involves lifting the epiglottis and endotracheal tube, passing by the vocal cords, and exerting a strong stimulation to the trachea. This results in an elevated level of catecholamine and consequent increases in blood pressure (BP)

and heart rate (HR), exerting a negative influence on the patients' cardiovascular system [1,2]. Lightwand is a tool that can be utilized in patients with poor teeth conditions or difficulties in mouth opening due to temporomandibular joint problems. This tool allows for intubation without lifting the glottis using light wave [3]. Esmolol is a relatively cardiac-selective beta blocker with an extremely short onset and half-life [4,5]. Several studies have assessed the

dose of esmolol required to minimize hemodynamic changes, in case of intubation through direct laryngoscope [6,7]. On the other hand, for lightwand-based intubation, there was no study identifying the appropriate dose of esmolol. Thus, the authors of this study aimed to identify the effect of different doses of esmolol on hemodynamic changes and the appropriate dose of esmolol during lightwand intubation.

## MATERIALS AND METHODS

After obtaining study approval from the Institutional Review Board of Soonchunhyang university hospital (no. 2018-06-041-002), we recruited 140 patients of the American Society of Anesthesiologists class I and II who required general anesthesia for elective surgery.

Patients with hypertension, cardiac problems, cervical spine fracture, tumors, or polyps in the upper airway, those with expected airway difficulties, and patients currently using beta blockers were excluded from the study. Informed consent was obtained from all patients. Using a computerized random number generator ([www.random.org](http://www.random.org)), the patients were divided into four different groups; 35 subjects in each group. For the 'C' group, 20 ml of normal saline was prepared, while the 'E0.5', 'E1', and 'E2' groups had 20 ml of normal saline containing esmolol 0.5 mg/kg, 1 mg/kg, and 2 mg/kg, respectively.

The patients received intramuscular injections of glycopyrrolate 0.2 mg 30 min prior to entering the operation room (OR). After the patient was admitted to the OR, regular monitoring equipment including electrocardiography, non-invasive blood pressure, and pulse oximetry were attached, and baseline BP and HR were measured ( $T_B$ ).

The anesthesiologist performed pre-oxygenation with 100% oxygen for 3 min, followed by induction of anesthesia with intravenous (IV) propofol 2 mg/kg. Immediately before injecting propofol, 40 mg of lidocaine was injected. After the patient lost consciousness, rocuronium 0.6 mg/kg was injected, and BP and HR were measured ( $T_1$ ). Immediately after the injection of rocuronium, either 20 ml of normal saline or 20 ml of normal saline containing 0.5 mg/kg, 1 mg/kg, or 2 mg/kg of esmolol were injected over 15–20 s.

Two minutes after the injection of the study drug, we performed lightwand (Flexible Lighted Stylets, Bovie Medical Corporation, USA) intubation with an assistant performing jaw-lift. All lights in the OR were turned off to ensure darkness in the room, until the lightwand passed by

the oral cavity and showed the brightest luminescence in the midline of the anterior neck. Using the light, an endotracheal tube was inserted into an appropriate position, and the lightwand was removed. Capnography and stethoscopes were used to confirm that the endotracheal tube was correctly inserted into the trachea. One minute after intubation, BP and HR were measured ( $T_1$ ). Cases involving an intubation time over 15 s or  $\geq 3$  attempts were considered as failures. To eliminate the differences due to technical expertise, all intubations were conducted by a single experienced anesthesiologist who performed  $\geq 500$  cases of intubation using the lightwand. Anesthesia was maintained using 2% sevoflurane, and medical air and oxygen were used to maintain  $FiO_2$  0.45. BP and HR were measured at 3 min ( $T_3$ ), 5 min ( $T_5$ ), and 10 min ( $T_{10}$ ) post-intubation. In addition, rate-pressure product (RPP)—an index of myocardial oxygen consumption calculated by multiplying systolic blood pressure (SBP) and HR—was calculated at each time point:  $T_B$ ,  $T_1$ ,  $T_3$ ,  $T_5$  and  $T_{10}$ .

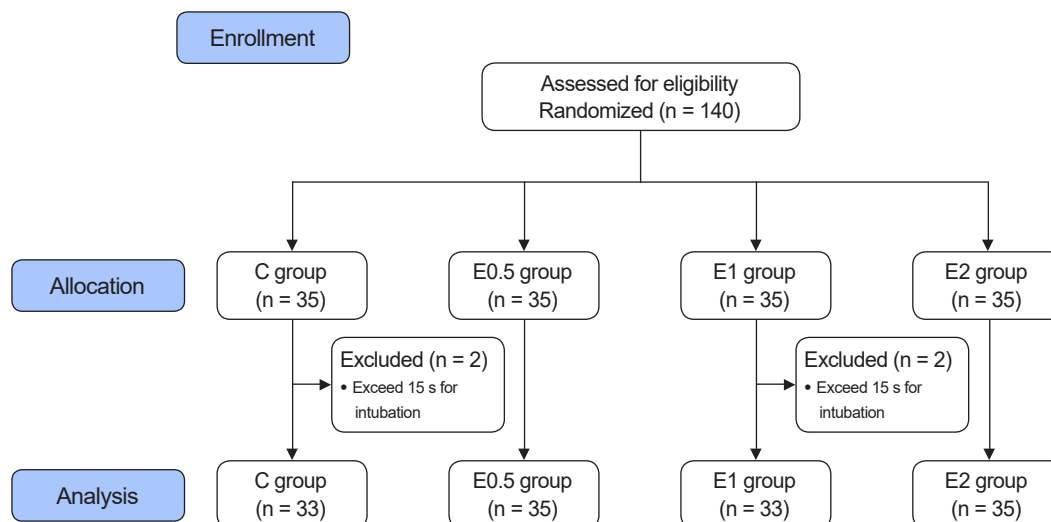
Prior to anesthesia, the investigator prepared the drug in advance. The nurse who injected the drug and anesthesiologist were not able to know the dose of esmolol for ensuring double-blinded study.

The data were compiled using SPSS 25.0 for Windows (IBM Co., USA) and were presented as mean  $\pm$  standard deviation where appropriate. First, the Kolmogorov-Smirnov test was used to determine if the values showed a normal distribution. The values with a normal distribution (weight, body mass index, SBP, mean blood pressure [MBP]) were analyzed using ANOVA and age, diastolic blood pressure (DBP), HR, RPP were analyzed using the Kruskal-Wallis test. Categorical data were analyzed using the chi-square test. The probability value of  $< 0.05$  was regarded as statistically significant.

## RESULTS

Two patients from each the C group and E1 group were excluded from the study due to their intubation time exceeding 15 s. In the end, 136 patients were included in this study (Fig. 1). There were no noticeable differences in patient characteristics among the different groups (Table 1). Furthermore, there were no differences in the initial measurements of SBP, DBP, MBP, HR and RPP immediately after entering the OR ( $T_B$ ) (Table 2).

For SBP, DBP, and MBP, there were no significant differences among the groups before and after intubation (Figs. 2–4).



**Fig. 1.** Flowchart illustrating the selection of patients. C: control, E0.5: esmolol 0.5 mg/kg, E1: esmolol 1.0 mg/kg, E2: esmolol 2.0 mg/kg.

**Table 1.** Demographic Data

Variable	C group (n = 33)	E0.5 group (n = 35)	E1 group (n = 33)	E2 group (n = 35)
Sex (M/F)	13/20	16/19	12/21	13/22
Age (yr)	39.9 ± 11.8	40 ± 12.0	42.1 ± 12.5	43.3 ± 11.2
Weight (kg)	65.4 ± 15.3	64.9 ± 13.1	65.3 ± 12.6	64.6 ± 13.2
BMI (kg/m <sup>2</sup> )	24.6 ± 3.7	23.6 ± 2.9	24.1 ± 3.7	23.9 ± 3.4

Values are presented as number only or mean ± SD. C: control, E0.5: esmolol 0.5 mg/kg, E1: esmolol 1.0 mg/kg, E2: esmolol 2.0 mg/kg, BMI: body mass index.

**Table 2.** Hemodynamic Baseline Values

Variable	C group (n = 33)	E0.5 group (n = 35)	E1 group (n = 33)	E2 group (n = 35)
SBP (mmHg)	137.0 ± 21.0	137.9 ± 15.8	140.5 ± 18.8	140.4 ± 19.9
DBP (mmHg)	78.0 ± 11.4	78.7 ± 10.8	79.7 ± 14.7	82.9 ± 13.2
MBP (mmHg)	100.3 ± 13.6	101.6 ± 11.2	103.1 ± 13.9	106.0 ± 15.0
HR (beats/min)	74.4 ± 12.5	72.8 ± 15.4	74.0 ± 14.2	77.8 ± 14.2
RPP (mmHg × beats/min)	10,199.0 ± 2,257.8	10,035.8 ± 2,404.1	10,460.1 ± 2,823.8	10,964.8 ± 2,682.7

Values are presented as mean ± SD. C: control, E0.5: esmolol 0.5 mg/kg, E1: esmolol 1.0 mg/kg, E2: esmolol 2.0 mg/kg, SBP: systolic blood pressure, DBP: diastolic blood pressure, MBP: mean blood pressure, HR: heart rate, RPP: rate-pressure product.

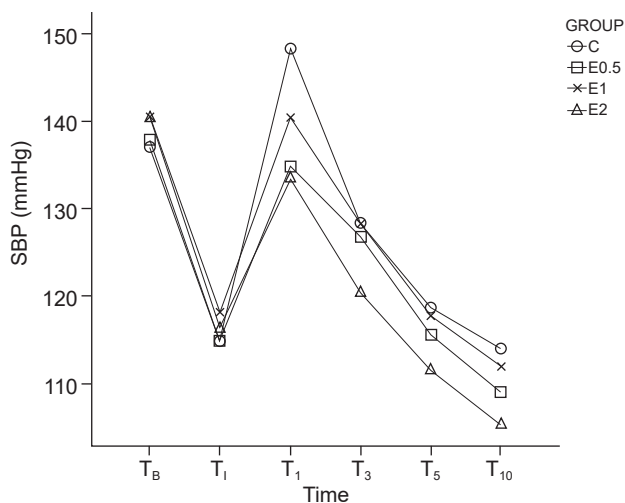
For HR, measurements 1 min after intubation ( $T_1$ ) were significantly different between the C group and E1 group (100.11 vs. 85.34,  $P \leq 0.001$ ), as well as 3 min after intubation ( $T_3$ ) (93.94 vs. 83.63,  $P = 0.02$ ). Similarly, there were significant differences between the C group and E2 group 1 min after intubation ( $T_1$ ) (100.11 vs. 87.09,  $P \leq 0.001$ ) and 3 min after intubation ( $T_3$ ) (93.94 vs. 81.97,  $P \leq 0.001$ ) (Fig. 5).

For RPP, there were significant differences between the C group and E2 group 1 min after intubation ( $T_1$ ) (15,003.43 vs. 11,665.40,  $P = 0.001$ ) and 3 min after intubation ( $T_3$ ) (12,162.37 vs. 9,861.89,  $P = 0.002$ ) (Fig. 6).

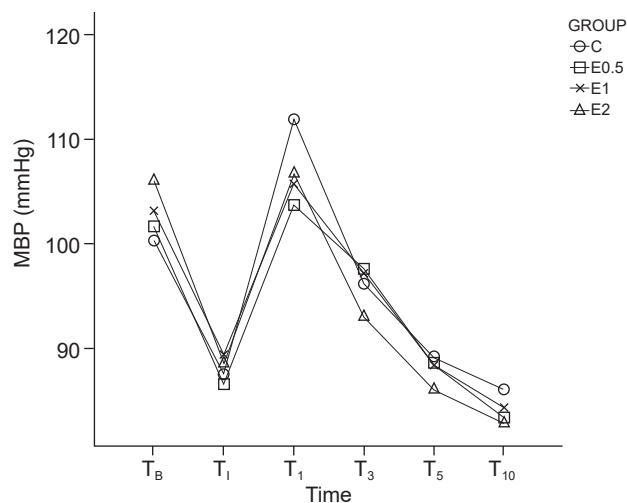
## DISCUSSION

The purpose of this study was to identify the effect of different doses of esmolol and the appropriate dose of esmolol on hemodynamic changes during lightwand intubation. For SBP, DBP, and MBP, there were no significant differences observed between the C group and E0.5, E1, and E2 groups. However, for HR, the level of elevation immediately after intubation was suppressed in the E1 and E2 groups compared to the C group. In addition, RPP significantly decreased in the E2 group compared to the C group.

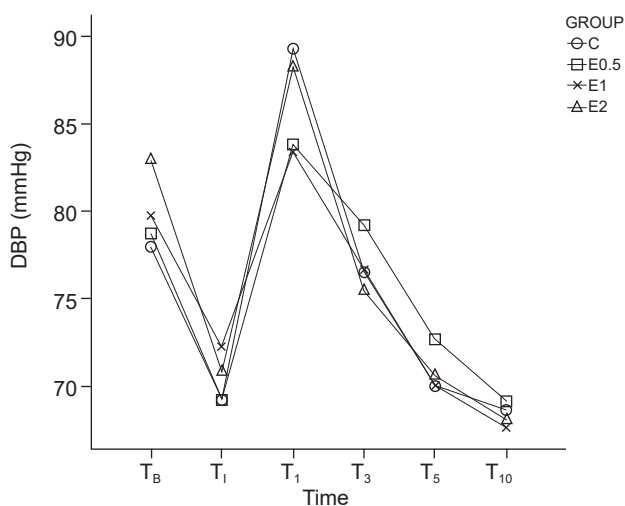
Intubation using a direct laryngoscope results in a strong



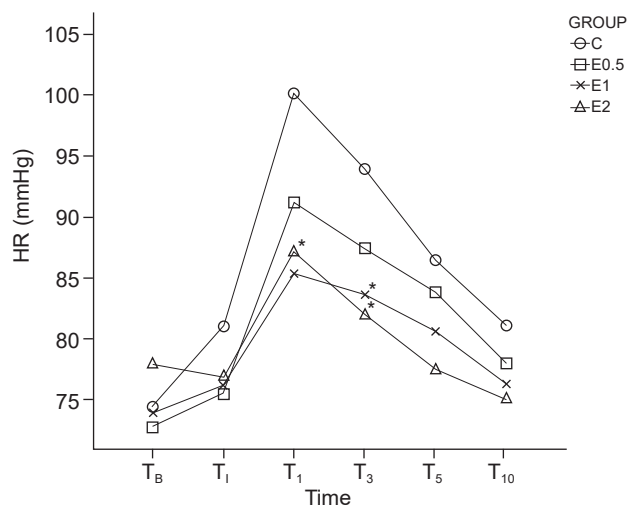
**Fig. 2.** SBP changes with lightwand intubation in the four patient groups. All values are expressed as mean values. C: control, E0.5: esmolol 0.5 mg/kg, E1: esmolol 1.0 mg/kg, E2: esmolol 2.0 mg/kg, SBP: systolic blood pressure, T<sub>B</sub>: before induction (baseline), T<sub>I</sub>: 2 min before intubation (induction), T<sub>1</sub>: 1 min after intubation, T<sub>3</sub>: 3 min after intubation, T<sub>5</sub>: 5 min after intubation, T<sub>10</sub>: 10 min after intubation.



**Fig. 4.** MBP changes with lightwand intubation in the four patient groups. All values are expressed as mean values. C: control, E0.5: esmolol 0.5 mg/kg, E1: esmolol 1.0 mg/kg, E2: esmolol 2.0 mg/kg, MBP: mean blood pressure, T<sub>B</sub>: before induction (baseline), T<sub>I</sub>: 2 min before intubation (induction), T<sub>1</sub>: 1 min after intubation, T<sub>3</sub>: 3 min after intubation, T<sub>5</sub>: 5 min after intubation, T<sub>10</sub>: 10 min after intubation.

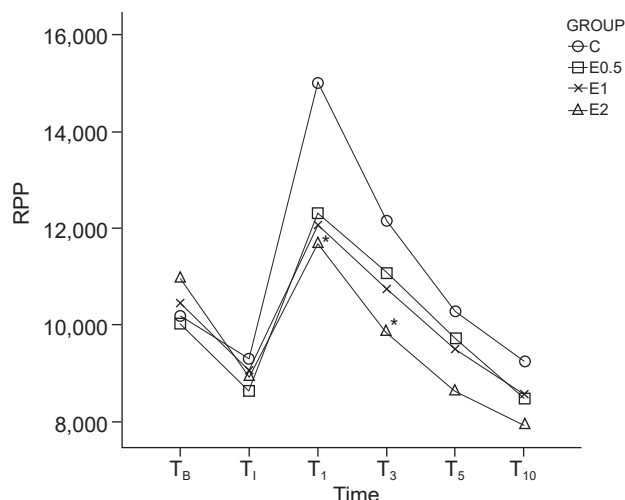


**Fig. 3.** DBP changes with lightwand intubation in the four patient groups. All values are expressed as mean values. C: control, E0.5: esmolol 0.5 mg/kg, E1: esmolol 1.0 mg/kg, E2: esmolol 2.0 mg/kg, DBP: diastolic blood pressure, T<sub>B</sub>: before induction (baseline), T<sub>I</sub>: 2 min before intubation (induction), T<sub>1</sub>: 1 min after intubation, T<sub>3</sub>: 3 min after intubation, T<sub>5</sub>: 5 min after intubation, T<sub>10</sub>: 10 min after intubation.



**Fig. 5.** HR changes with lightwand intubation in the four patient groups. Comparison of measurements in C group and E1 group showed significant differences in HR at 1 min after intubation (T<sub>1</sub>) (100.11 vs. 85.34,  $P \leq 0.001$ ), as well as at 3 min after intubation (T<sub>3</sub>) (93.94 vs. 83.63,  $P = 0.02$ ). Similarly, comparison of measurements in C group and E2 group demonstrated significant differences in HR at 1 min after intubation (T<sub>1</sub>) (100.11 vs. 87.09,  $P \leq 0.001$ ), as well as at 3 min after intubation (T<sub>3</sub>) (93.94 vs. 81.97,  $P \leq 0.001$ ). All values are expressed as mean values. C: control, E0.5: esmolol 0.5 mg/kg, E1: esmolol 1.0 mg/kg, E2: esmolol 2.0 mg/kg, HR: heart rate, T<sub>B</sub>: before induction (baseline), T<sub>I</sub>: 2 min before intubation (induction), T<sub>1</sub>: 1 min after intubation, T<sub>3</sub>: 3 min after intubation, T<sub>5</sub>: 5 min after intubation, T<sub>10</sub>: 10 min after intubation. \* $P < 0.05$  compared with C group.

stimulation of the larynx, resulting in an elevated level of catecholamine, and consequently, increased BP, HR, and RPP [1,2]. From a hemodynamic aspect, the elevated HR results in an increased oxygen consumption, especially in the patients with ischemic heart disease. This stimulates a negative effect on the myocardial oxygen balance, leading



**Fig. 6.** RPP changes with lightwand intubation in the four patient groups. Comparison of RPP measurements in C group and E2 group showed significant differences at 1 min after intubation (T<sub>1</sub>) (15,003.43 vs. 11,665.40,  $P = 0.001$ ) and 3 min after intubation (T<sub>3</sub>) (12,162.37 vs. 9,861.89,  $P = 0.002$ ). All values are expressed as mean values. C: control, E0.5: esmolol 0.5 mg/kg, E1: esmolol 1.0 mg/kg, E2: esmolol 2.0 mg/kg, RPP: rate-pressure product, T<sub>B</sub>: before induction (baseline), T<sub>1</sub>: 2 min before intubation (induction), T<sub>1</sub>: 1 min after intubation, T<sub>3</sub>: 3 min after intubation, T<sub>5</sub>: 5 min after intubation, T<sub>10</sub>: 10 min after intubation. \* $P < 0.05$  compared with C group.

to possible onset of myocardial ischemia during the surgery [8]. Moreover, RPP is a known, trustworthy indicator of myocardial oxygen demand [9,10].

The lightwand can be utilized in situations involving difficult airways, where intubation using direct laryngoscope is difficult or resulted as a failure. More specifically, the lightwand is useful in patients with a hard-to-open mouth, those with a high risk of teeth damage, or excessive secretion of saliva. Since intubation using the lightwand does not involve lifting the glottis, it exerts a weaker direct stimulation to the mouth and larynx [11], resulting in less pain in the neck area after anesthesia, and results in fewer cases of hoarseness or dysphasia [12,13]. Furthermore, its simple preparation process, exceptional mobility, and easy-to-clean characteristics are additional benefits [3].

The previous study by Takahashi et al., which assessed young and healthy patients, showed no difference in changes of HR, SBP, and DBP between the lightwand and direct laryngoscope intubation [14]. Similarly, Yoon et al. [15] also demonstrated that changes in HR and MBP were similar between the two procedures when performing intubation in patients with cerebral aneurysms. Several studies have supported these findings, showing little to no dif-

ference in the trend of hemodynamic changes [12–16]. Meanwhile, Salgado et al. claimed that the lightwand blunted the elevation of MBP [17], and Nishikawa et al. [11] showed blunted elevation of SBP using the lightwand in a cohort of normal patients.

Esmolol used in this study is a beta1-selective adrenergic receptor blocking agent, which is an anti-hypertensive drug that reaches peak blood concentration within 2 min and has an extremely short half-life of ~9 min [4]. Esmolol has existed for a long time for intubation using direct laryngoscope. The previous study by Kindler et al. [18] confirmed that the groups treated with 1 mg/kg and 2 mg/kg of esmolol exhibited blunted hemodynamic changes when using laryngoscope compared to the placebo group. A single injection of esmolol 100 mg prior to intubation using laryngoscope resulted in lesser hemodynamic changes compared to the control group [19], and the same outcome was deduced with an injection of esmolol 150 mg [20]. Furthermore, another study has shown that a bolus injection of esmolol 1 mg/kg prior to intubation and continuous infusion at 150  $\mu$ g/kg/min also resulted in blunted hemodynamic changes. [21] Overall, multiple studies with various designs have been performed thus far.

As mentioned above, there have been several studies suggesting a similar level of hemodynamic changes during intubations with either a lightwand or direct laryngoscope [12,14–16]. Nonetheless, the studies of appropriate dose of esmolol usage during lightwand intubation were not found by authors. The actual results showed that 1–2 mg/kg of esmolol effectively reduced HR, while RPP blunting was most effective with 2 mg/kg of esmolol. These values are near the recommended dose of esmolol during direct laryngoscope intubation, according to the above-mentioned study by Kindler et al. [18]. These findings imply that despite using the lightwand, the level of stimulation was comparable to that of direct laryngoscope intubation. In addition, these findings can be considered that the major cause of hemodynamic changes is the direct stimulation of the trachea by the endotracheal tube rather than direct stimulation via lifting the glottis with the laryngoscope [14].

The level of hemodynamic changes from lightwand intubation will likely be associated with technical expertise. A Prolonged procedure time or repeated attempts will result in the tip of the lightwand exerting a strong stimulation to the larynx, especially in piriform recess and epiglottic val- lecular. This causes blood catecholamine levels to increase even further [11]. Moreover, patients with hypertension ex-



hibit a greater increase of blood catecholamine levels with the same level of stimulation, resulting in greater hemodynamic changes [22,23]. Last, patients with difficult airway will likely exhibit a greater elevation of BP and HR due to the lengthened procedure time or repeated attempts. In this study, all procedures were performed by an expert anesthesiologist who performed lightwand intubation > 500 times. There was no case that involved more than 2 failures and only 4 cases required  $\geq 15$  seconds of procedure time.

When performing lightwand intubation, having an assistant to lift the patients' mandibular angle to open their mouth will make the procedure more convenient to complete [3]. Thus, in this study, the jaw-lift method was utilized. On the other hand, a single anesthesiologist opening the patient's mouth with one hand and manipulating the lightwand with the other hand makes it difficult to ensure neck extension. And lights may not be clearly visible due to neck folds. Consequently, the procedure may take longer and exhibit a greater chance of failure.

Although we have performed IV injections of lidocaine 40 mg—which is known to reduce the cough reflex—prior to the injection of propofol, the effect from lidocaine would have been negligible since the typical dosage for lidocaine to see its effectiveness is much greater [24].

There are a few limitations in this study. First, we did not measure blood catecholamine levels in each group. Adrenergic hormone is the key factor of BP and HR elevation, and the measurements may have provided meaningful results. Second, due to the intermittent measurement of blood pressure, the time point of maximal changes may have been undetected. For an accurate assessment, measurement of continuous arterial blood pressure should have been considered. Third, we could not assess post-intubation complications such as sore throat and hoarseness. These complications are prevalent during intubation with direct laryngoscope, and the use of a lightwand is reported to reduce these complications. However, in this study, we could not address this issue. This study was based on a cohort of healthy patients aged 18–50 years old without cardiovascular diseases. Additional studies should be performed on the patients with cardiovascular diseases, including hypertension.

In conclusion, during lightwand intubation, a single injection of 1–2 mg/kg esmolol resulted in blunted HR elevation, and 2 mg/kg of esmolol was sufficient to suppress RPP elevation.

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## CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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