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Effect of remifentanil infusion on the hemodynamic response during induction of anesthesia in hypertensive and normotensive patients: a prospective observational study

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Abstract

Background: The induction of general anesthesia may cause hemodynamic instability. Remifentanil is often administered to suppress the hemodynamic response. We aimed to evaluate the effect of remifentanil infusion on the hemodynamic response to induction of anesthesia in hypertensive and normotensive patients.

Methods: Patients were divided into two groups: Group H (n = 102) were hypertensive patients and Group C (n = 107) were normotensive patients. During induction, all patients received 1 μg/kg of remifentanil as a loading dose over 2 minutes, followed by a continuous infusion at 0.05 μg/kg/minute. We analyzed the systolic, diastolic, and mean pressures and heart rate pre-induction, pre-intubation, immediately post-intubation, and at 2, 4, 6, 8, and 10 minutes after intubation.

Results: The systolic, diastolic, and mean pressures before induction were significantly higher in group H compared with group C, but there was no significant difference between the two groups immediately after intubation. Blood pressures immediately after intubation were similar to the pre-induction blood pressure. There was no significant difference in heart rate between the two groups at any time point.

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Conclusions: Remifentanil infusion effectively attenuates the hemodynamic response to induction of general anesthesia in hypertensive and normotensive patients.

Keywords
General anesthesia, hemodynamic changes, hypertension, remifentanil, tracheal intubation, systolic blood pressure, diastolic blood pressure

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Introduction

During induction of general anesthesia, endotracheal intubation may lead to hemodynamic instability. Manipulation of the laryngoscope, insertion of the endotracheal tube, and pain during intubation stimulate the autonomic nervous system, causing hypertension and tachycardia.[1] Additionally, hypotension frequently occurs immediately before and soon after tracheal intubation until commencement of the surgical procedure because of the vasodilator and central nervous system depressant effects of anesthetic agents.[2] Hemodynamic instability is more severe in patients with hypertension and heart disease.[3,4] It is crucial to minimize hemodynamic changes during induction of general anesthesia because excessive hemodynamic instability may lead to myocardial ischemia or worsen tissue perfusion and adversely impact patient prognosis, particularly in patients with hypertension and heart disease. The hemodynamic instability during this period can be mitigated with the appropriate use of hypnotics and analgesics.[5,6]

Inhalational anesthetic agents have hypnotic and analgesic effects, and may prevent hemodynamic changes that result from intubation; however, high concentrations are required when they are used alone.[7] Additionally, high concentrations of inhalational anesthetic agents can cause vasodilation and cardiovascular depression, leading to a profound decrease in blood pressure before intubation and soon after induction.[2] The use of opioids in combination with inhalational anesthetic agents can minimize hemodynamic instability by reducing cardiovascular depression, and it provides adequate pain relief at a lower inhalational anesthetic agent concentration.[6]

Remifentanil is an opioid analgesic with a rapid onset and short duration of action and it has recently been widely used in combination with inhalational and intravenous anesthetic agents.[8–10] In adult patients, administration of remifentanil (1 μg/kg) during induction of anesthesia has been shown to reduce the hemodynamic response to intubation.[10–12] Maruta et al.[13] reported that bolus doses or a continuous infusion of remifentanil that attenuated the hemodynamic response was similar in both normotensive and hypertensive patients with or without the use of antihypertensive medication. However, no large-scale study has been performed to evaluate the differences in the hemodynamic response during induction of general anesthesia between normotensive and hypertensive patients. In particular, few studies have compared the effects of a continuous infusion of low-dose remifentanil among normotensive and hypertensive patients. The aim of this study was to evaluate the effect of a

continuous remifentanil infusion on the hemodynamic response to intubation among hypertensive and normotensive patients.

Methods

Study population

We conducted this prospective observational study in American Society of Anesthesiologists (ASA) class I and II patients who were between 40 and 65 years old and who were scheduled to undergo general anesthesia with endotracheal intubation. The study was approved by the Institutional Review Board of Hanyang University Seoul Hospital (approval number 2016-09-019-004, approval date November 23, 2016), and was registered in a public trial registry at the Clinical Research Information Service (https: //cris.nih.go.kr/cris/index.jsp) (KCT0002290).

We obtained informed consent from all study patients. Patients who did not provide consent and those who were expected to have a difficult intubation were excluded from the study. Patients with severe cardiac insufficiency or pulmonary disease, uncontrolled hypertension, and hemodynamic instability, including shock, bradycardia, or arrhythmia, were excluded. We also excluded patients with a body mass index (BMI) greater than 30 kg/m^2, impaired conscious level, and cognitive dysfunction.

Study protocol and anesthetic technique

We divided the patients into two groups. Patients who were previously diagnosed with hypertension and who were currently taking antihypertensive medication were assigned to the hypertensive group (Group H). Patients with no previous history of hypertension were assigned to the control group (Group C). Antihypertensive agents, except angiotensin-converting enzyme inhibitors and angiotensin receptor blockers, were continued until the day of surgery. Remifentanil was prepared at a concentration of 50 μg/mL in a 50-mL syringe. All patients were premedicated with midazolam (0.05 mg/kg intravenously) and atropine sulfate (0.5 mg intramuscularly) on the ward 30 minutes before induction. In the operating room, vital signs were monitored using a continuous electrocardiogram (ECG), non-invasive blood pressure (NIBP), and pulse oximetry. The level of consciousness and the depth of anesthesia were monitored using a bispectral index (BIS) monitor (2000A, Aspect Medical Systems Inc., Norwood, MA, USA). After intravenous administration of 100 mL of crystalloid before the induction of anesthesia,[14] fluid infusion was continued at 180 mL/hour. Induction of anesthesia was performed using intravenous propofol (1–1.2 mg/kg) and manual ventilation was commenced with 6 L/minute of 100% oxygen and inhalational anesthesia using 2.0 vol% of sevoflurane. After confirming loss of consciousness, neuromuscular blockade was established with rocuronium (0.6 mg/kg, intravenously). Remifentanil (1 μg/kg), based on the calculated ideal body weight, was administered as a loading dose over 2 minutes using a syringe pump immediately after the intravenous administration of rocuronium. Remifentanil was continued as an intravenous infusion at 0.05 μg/kg/minute followed by endotracheal intubation. We calculated the effect-site concentration of remifentanil using the Minto formula[8] to compensate for these differences.

If the heart rate decreased to less than 45 beats per minute for more than 1 minute, 0.5 mg of atropine sulfate was administered intravenously. If the systolic blood pressure (SBP) was less than 80 mmHg or the mean blood pressure (MBP) was less than 55 mmHg for more than 2 minutes, the

hypotension was corrected by intravenous administration of a vasopressor agent (ephedrine, 5–10 mg).

Outcome variables

The MBP, SBP, diastolic blood pressure (DBP), and heart rate of all patients were recorded at eight time points, as follows: before induction, immediately before intubation, immediately after intubation, and at 2, 4, 6, 8, and 10 minutes after intubation. The minimal alveolar concentration (MAC), end-tidal inhalational sevoflurane concentration, and BIS values were also recorded. The MAC was automatically calculated using an anesthetic machine (Dräger Primus®, Därger Medical, Lübeck, Germany) and it was adjusted for age. We evaluated recall of induction among patients postoperatively when they were fully awake.

Statistical analysis

Alanoglu et al.[11] reported hemodynamic changes during intubation using a 1 μg/kg loading dose of remifentanil. In this study, the MBP was 103.25 ± 25 mmHg in adult patients immediately after induction. Based on this study, we calculated the sample size using PASS software (Power analysis and sample size 14, NCSS, LLC., Kaysville, UT, USA). A sample size of 100 patients per group was required for 80% power with a p-value of <0.05 for a type 1 error to detect a change of 10 mmHg in the MBP between groups ($\alpha = 0.05$, $\beta = 0.2$). Allowing for a 10% dropout rate, we included 111 patients in each group.

We used SigmaStat® for Windows Version 3.5 (Systat Software Inc., San Jose, CA, USA) for statistical analysis. Data were presented as the number of patients or mean ± standard deviation. Continuous variables were compared using the Mann–Whitney U test or an independent *t*–test. The Shapiro–Wilk test was used to test for normality of the variable distribution. Categorical values were compared using the Chi-squared test. A repeated measures analysis of variance (ANOVA) was performed to analyze changes within groups for SBP, DBP, MBP, and heart rates at pre-induction, pre-intubation, immediately after intubation, and at 2, 4, 6, 8, and 10 minutes after intubation. A post-hoc analysis was performed using the Tukey's b(K) method. Data were considered to be significant if the p-value was less than 0.05 (two-tailed).

Results

Study population

This study was conducted from December 30, 2016 to May 8, 2017. There were 222 patients screened and classified into group C ($n = 111$) or group H ($n = 111$). As shown in Figure 1, four patients were excluded from group C and nine patients were excluded from group H. Thus, 107 patients were included in group C and 102 patients were included in group H.

There were no significant differences between the two groups regarding body weight, height, duration of anesthesia, and duration of surgery. However, the BMI, age, and ASA class were significantly different between groups ($P = 0.011$; $P < 0.001$; $P < 0.001$, respectively; Table 1).

Mean blood pressure

The MBP was significantly higher in group H compared with group C before induction, before intubation, and 2 minutes after intubation ($P < 0.001$, $P = 0.011$, and $P = 0.009$, respectively; Figure 2). However, there was no difference in MBP between the two groups immediately after intubation and at 4 minutes after intubation. In both groups, MBP immediately after intubation

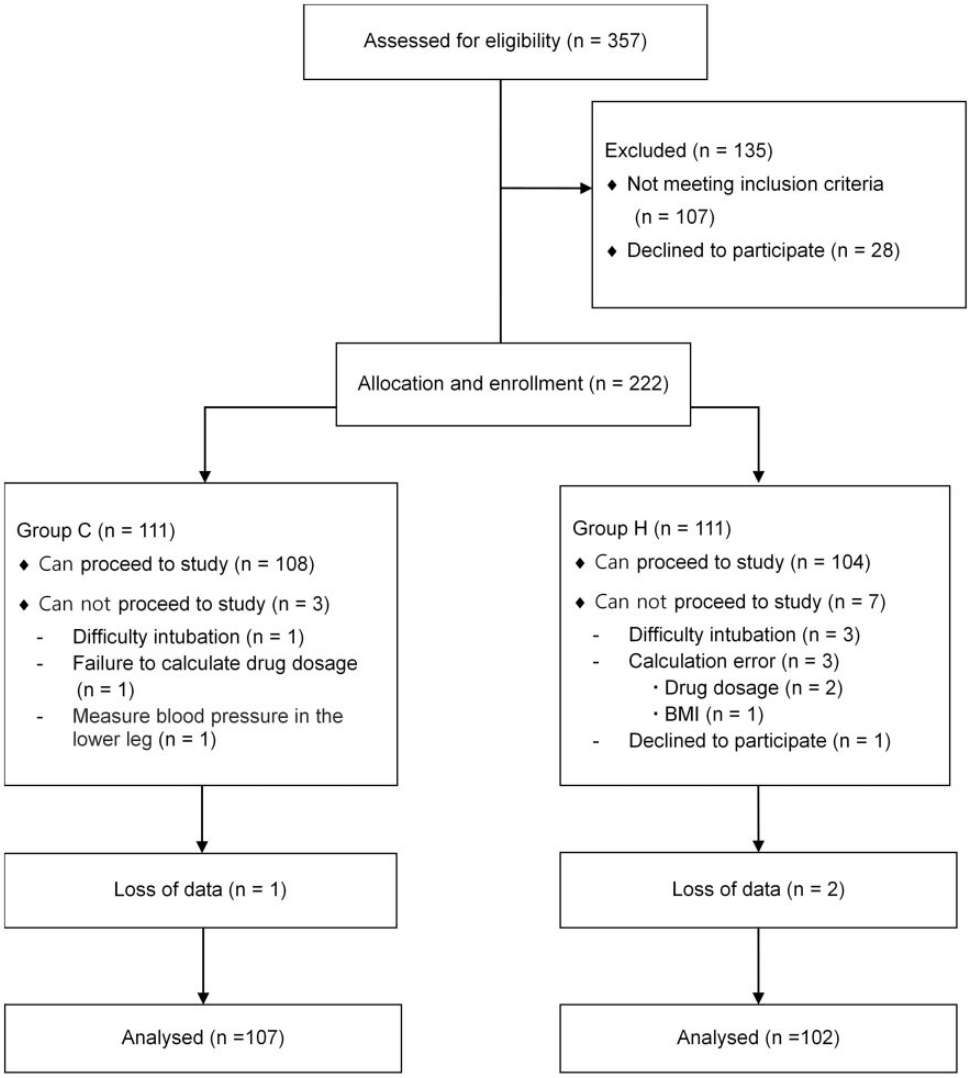

Figure 1. Flow diagram of patient recruitment and exclusion criteria.

was similar to the pre-induction blood pressure. The MBP was significantly lower before intubation and at 2 minutes after intubation, which was in contrast to pre-induction values ($P < 0.001$ at all time points). The percentage change in MBP was significantly higher in group H compared with group C beginning at 4 minutes after intubation (Table 2).

Systolic blood pressure

SBP was significantly higher in group H compared with group C before induction and at 2 minutes after intubation ($P < 0.001$ and $P = 0.022$, respectively; Figure 3). In both groups, the SBP immediately after intubation was lower than the pre-induction SBP. The SBP was

Table 1. Demographic data.

	Group C (n = 107)	Group H (n = 102)	P-value*
Age[c]	51.6 ± 6.7	57.0 ± 0.6	<0.001
Sex (Male/Female)[a]	40/67	44/58	0.271
Height (cm)[c]	162.4 ± 8.5	160.8 ± 8.5	0.838
Weight (kg)[b]	63.0 ± 10.8	64.8 ± 11.8	0.267
BMI (kg/m^2)[c]	23.8 ± 2.8	24.9 ± 3.6	0.011
Anesthesia time (min)[c]	155.3 ± 93.7	142.8 ± 85.1	0.316
Operation time (min)[c]	116 ± 89.8	100.5 ± 76.6	0.177
ASA class (1/2)[a]	71/36	4/98	<0.001

Values are presented as the number or the mean ± SD. [a]Chi-squared test, [b]Independent *t*-test, [c]Mann–Whitney U test. BMI, body mass index; ASA, American Society of Anesthesiologists physical status classification system.

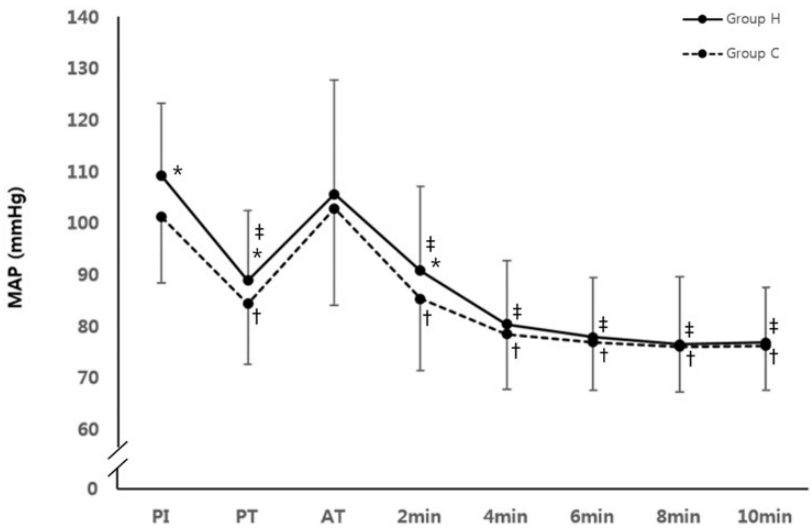

Figure 2. Changes in the mean arterial pressure (MAP). PI, pre-induction; PT, pre-tracheal intubation; AT, after tracheal intubation; 2 min, 2 minutes after intubation; 4 min, 4 minutes after intubation; 6 min, 6 minutes after intubation; 8 min, 8 minutes after intubation; 10 min, 10 minutes after intubation. Data were analyzed using a repeated measures ANOVA. *$P < 0.05$ compared with group C; †$P < 0.05$ compared with PI in group C; ‡$P < 0.05$ compared with PI in group H.

significantly lower before intubation and at 2 minutes after intubation compared with the pre-induction SBP ($P < 0.001$ at all time points). The percent change in SBP was significantly higher in group H compared with group C at all time points except 2 minutes after intubation (Table 2).

Diastolic blood pressure

DBP was significantly higher in group H compared with group C before induction, just before intubation, and at 2 and 8 minutes after intubation ($P = 0.007$, $P = 0.003$, $P = 0.026$, and $P = 0.041$,

Table 2. The percent changes in the variable hemodynamic parameters compared with the pre-induction value.

	PI-PT	PI-AT	PI-2	PI-4	PI-6	PI-8	PI-10
MBP							
Group C (%)	16.1 ± 10.2	−2.7 ± 20.3	15.0 ± 14.5	21.7 ± 11.8	23.3 ± 10.6	24.1 ± 10.7	23.9 ± 10.5
Group H (%)	17.9 ± 12.8	2.3 ± 22.1	16.0 ± 16.7	25.6 ± 12.6	28.0 ± 11.7	29.2 ± 12.9	30.0 ± 13.0
P-value	0.265[a]	0.088[b]	0.641[b]	0.022[a]	0.003[a]	0.002[a]	<0.001[a]
SBP							
Group C (%)	15.5 ± 0.9	1.6 ± 1.7	14.8 ± 1.4	21.3 ± 1.2	23.3 ± 1.0	24.1 ± 0.9	23.9 ± 0.9
Group H (%)	20.0 ± 1.3	8.2 ± 1.7	17.3 ± 1.5	26.8 ± 1.0	29.3 ± 1.0	30.0 ± 1.0	31.3 ± 1.1
P-value	0.001[b]	0.007[a]	0.113[b]	<0.001[b]	<0.001[a]	<0.001[a]	<0.001[b]
DBP							
Group C (%)	16.1 ± 1.2	−5.9 ± 2.2	14.5 ± 1.6	21.9 ± 1.4	18.0 ± 6.53	24.9 ± 1.1	24.4 ± 1.1
Group H (%)	15.0 ± 1.6	−3.2 ± 2.6	14.0 ± 1.9	22.9 ± 1.4	25.6 ± 1.4	25.9 ± 1.2	27.5 ± 1.4
P-value	0.728[b]	0.186[b]	0.720[b]	0.298[b]	0.151[b]	0.458[b]	0.068[b]
HR							
Group C (%)	−2.4 ± 1.5	−23.8 ± 2.4	−12.3 ± 2.0	−1.1 ± 1.5	−58.1 ± 2.4	−3.5 ± 1.6	−3.4 ± 1.5
Group H (%)	1.1 ± 1.3	−17.4 ± 2.5	−7.6 ± 1.8	−7.4 ± 1.7	−5.1 ± 1.5	−0.7 ± 1.6	1.1 ± 1.4
P-value	0.239[b]	0.027 [b]	0.107[b]	0.006[a]	<0.001[b]	0.037[b]	0.031[a]

Values are presented as the mean ± standard error (SE). Data were analyzed using an [a]Independent *t*-test or the [b]Mann–Whitney U test after a normality test. PI-PT, % change of mean arterial pressure at pre-intubation compared with pre-induction; PI-AT, % change of mean arterial pressure just after intubation compared with pre-induction; PI-2, % change of mean arterial pressure at 2 minutes after intubation compared with pre-induction; PI-4, % change of mean arterial pressure at 4 minutes after intubation compared with pre-induction; PI-6, % change of mean arterial pressure at 6 minutes after intubation compared with pre-induction; PI-8, % change of mean arterial pressure at 8 minutes after intubation compared with pre-induction; PI-10, % change of mean arterial pressure at 10 minutes after intubation compared with pre-induction.

respectively; Figure 4). However, there was no difference between the two groups immediately after intubation. In both groups, DBP was significantly lower before intubation and at 2 minutes after intubation ($P < 0.001$ at all time points). In group H, unlike group C, there was no significant difference in DBP between immediately after intubation and pre-induction. The percentage change in DBP was not significantly different in both groups at all time points (Table 2).

Heart rate

There was no statistically significant difference in heart rate between the two groups at any time point (Figure 5). In both groups, the heart rate increased significantly immediately after intubation compared with pre-induction values ($P < 0.001$) and stabilized 8 minutes after intubation.

Other outcome variables

There was no statistically significant difference between the two groups in BIS, MAC, and the end-tidal sevoflurane concentration at any time point. The plasma concentration of remifentanil was high in hypertensive patients (group H: 7.4 ± 0.9 ng/mL, group C: 6.95 ± 0.8 ng/mL, $P < 0.001$), but there was no difference in the effect-site concentration between the two groups (group H: 3.2 ± 0.5 ng/mL, group C: 3.2 ± 0.3 ng/mL). Ephedrine and atropine use was also similar between the two groups (Table 3). After regaining consciousness in the recovery room, none of the patients

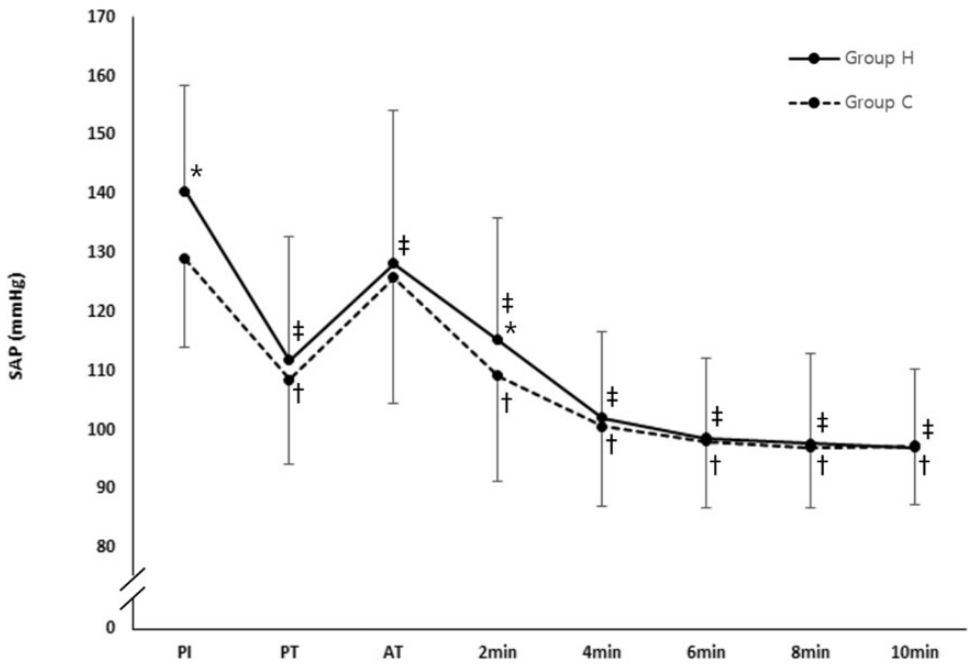

Figure 3. Changes in the systolic arterial pressure (SAP). PI, pre-induction; PT, pre-tracheal intubation; AT, after tracheal intubation; 2 min, 2 minutes after intubation; 4 min, 4 minutes after intubation; 6 min, 6 minutes after intubation; 8 min, 8 minutes after intubation; 10 min, 10 minutes after intubation. Data were analyzed using a repeated measures ANOVA. *$P < 0.05$ compared with group C; †$P < 0.05$ compared with PI in group C; ‡$P < 0.05$ compared with PI in group H.

reported recall of anesthesia induction or the surgical procedure.

Discussion

We analyzed the effect of remifentanil on the hemodynamic response to general anesthesia induction in hypertensive and normotensive patients. We found that a loading dose of 1 μg/kg of remifentanil administered over 2 minutes effectively inhibited the excessive increase of blood pressure and heart rate in hypertensive and normotensive patients.

Several studies[10–12] have reported that the hemodynamic changes related to tracheal intubation can be adequately controlled with a loading dose of remifentanil (1 μg/kg) that is administered over 30 seconds during induction of anesthesia in adult patients. However, others[15–17] have reported adverse effects, including severe bradycardia and hypotension, at similar or lower doses. In studies that reported adverse effects, the authors recommend slowing the rate of remifentanil infusion to lower the total dose or using vagolytic drugs to prevent bradycardia and hypotension. The contrasting results observed in the above studies may be related to the presence of co-morbidities, including cardiovascular disease. In the present study, in contrast to previous studies, we administered remifentanil as an infusion at a rate of 0.05 μg/kg/minute after a loading dose of 1 μg/kg over 2 minutes. We considered this to be an appropriate dose, keeping in mind the more profound hemodynamic changes

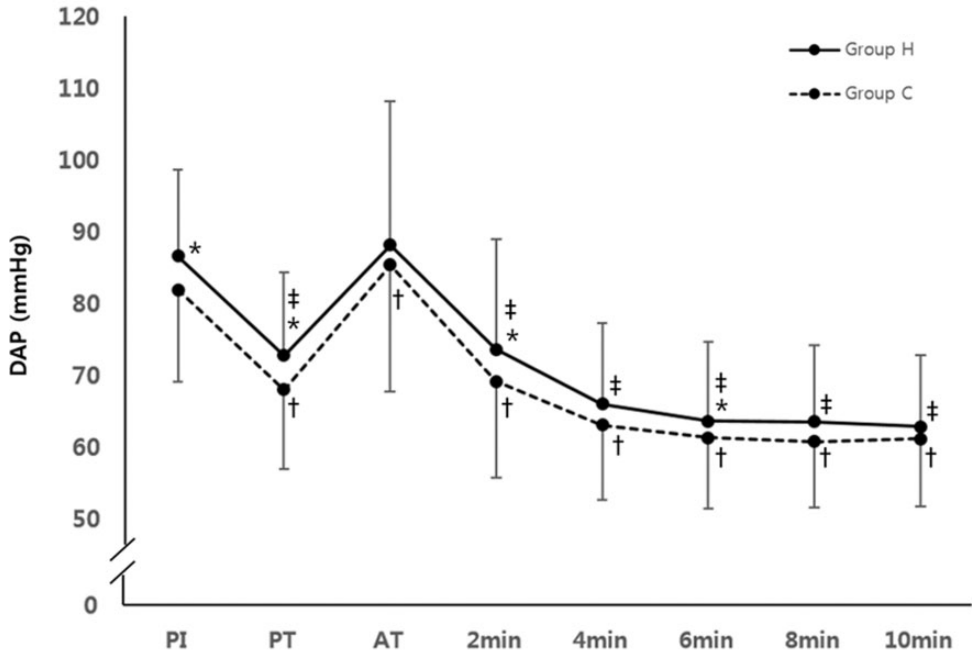

Figure 4. Changes in the diastolic arterial pressure (DAP). PI, pre-induction; PT, pre-tracheal intubation; AT, after tracheal intubation; 2 min, 2 minutes after intubation; 4 min, 4 minutes after intubation; 6 min, 6 minutes after intubation; 8 min, 8 minutes after intubation; 10 min, 10 minutes after intubation. Data were analyzed using a repeated measures ANOVA. *$P < 0.05$ compared with group C; †$P < 0.05$ compared with PI in group C; ‡$P < 0.05$ compared with PI in group H.

that are observed in hypertensive patients on antihypertensive medication, who often have underlying cardiovascular disease.

In the present study, despite a loading dose of 1 μg/kg of remifentanil that was administered over 2 minutes, the blood pressure values in the normotensive group were similar to those in a previous study by Alanoğlu et al.[11] However, the degree of blood pressure reduction was greater in the present study. We believe that the greater reduction in blood pressure values observed in our study was because our patients were older; the mean age of our study population was 10 years older than the patients in the study by Alanoğlu et al.[11] The elasticity of blood vessels decreases and the hemodynamic response to drugs or stimuli becomes more pronounced with increasing age.[3,4] Another possible reason for the greater reduction in blood pressure that was observed in our study could be because of the relatively low volume of intravenous fluid loading we used before induction. Maruta et al.[13] compared the effect of a continuous infusion with bolus administration of remifentanil and evaluated the reason in treated and untreated subgroups of hypertensive patients. They reported that a continuous infusion of remifentanil in contrast to bolus administration maintained baseline blood pressures for a prolonged duration after intubation in hypertensive patients, regardless of antihypertensive drug administration. Our findings are consistent with these findings; we observed fewer profound hemodynamic

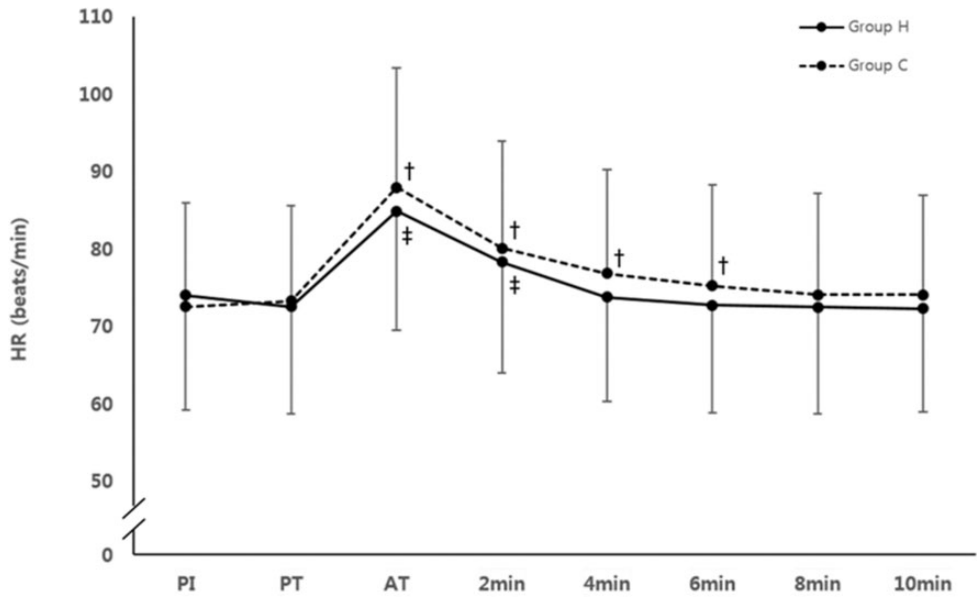

Figure 5. Changes in the heart rate (HR). PI, pre-induction; PT, pre-tracheal intubation; AT, after tracheal intubation; 2 min, 2 minutes after intubation; 4 min, 4 minutes after intubation; 6 min, 6 minutes after intubation; 8 min, 8 minutes after intubation; 10 min, 10 minutes after intubation. Data were analyzed using a repeated measures ANOVA. *$P < 0.05$ compared with group C in group H; †$P < 0.05$ compared with PI in group C; ‡$P < 0.05$ compared with PI in group H.

Table 3. Drugs administered for bradycardia or hypotension.

	Group C (n = 107)	Group H (n = 102)	P-value
Atropine	0 (0%)	0 (0%)	1.0
Ephedrine			
5 mg	6 (5.6%)	8 (7.8%)	0.158
10 mg	0 (0%)	3 (2.9%)	

Values are presented as the number (%). Data were analyzed using the Chi-squared test.

changes when remifentanil was administered as a continuous infusion.

We observed that remifentanil infusion leads to a decrease in blood pressure and heart rate. However, there was no incidence of bradycardia, and the heart rate was significantly higher in the normotensive group. The absence of remifentanil-induced bradycardia was probably a result of premedication with 0.5 mg of atropine sulfate that was administered intramuscularly 30 minutes before induction.

In hypertensive patients, smooth muscle cell de-differentiation causes arterial wall hypertrophy and increased distensibility.[18,19] Progressive arteriosclerosis in these patients leads to an exaggerated change in blood pressure and heart rate during induction of anesthesia and tracheal intubation.[20] Hypertensive patients are commonly treated with calcium channel blockers, diuretics, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or beta-blockers. These drugs induce arterial vasodilation, myocardial depression, inhibit the compensatory vasoconstrictor response, and reduce the blood volume,[21] which may affect the response to remifentanil. We observed that the change in blood pressure was marginally greater in the hypertensive group compared with

pre-induction values. This led to similar blood pressure values in both groups over time. We included ASA class I or II patients and excluded patients with severe cardiac dysfunction. Thus, we may have excluded patients with uncontrolled hypertension and those who were not on antihypertensive medication. If we had included patients in ASA class III or higher, our study population would have included those with uncontrolled hypertension, leading to more pronounced hemodynamic changes compared with those that were observed. Previous studies have focused on increased blood pressure resulting from tracheal intubation. Similarly, in our study, blood pressures decreased in the absence of stimulation in most patients. Although we did not express blood pressure change as a percentage, previous studies showed a change of more than 20% in the control group[10] and 25% to 30% in the hypertensive group.[21,22] Low blood pressures may lead to tissue hypoperfusion followed by secondary complications such as worsening heart disease. Thus, it is important to maintain blood pressures within the normal range. At 4 minutes after intubation, blood pressure values changed by more than 20% compared with pre-induction values in both groups. Therefore, active measures should be taken to minimize hypotension, including fluid administration, use of vasoconstrictors, and commencement of surgery without delay after induction of anesthesia.

Our study showed significant differences in age, BMI, and ASA class between the control and hypertensive groups. Aging can have a significant effect on cardiovascular function because it leads to blood vessel stiffening and hypertension.[23] Additionally, BMI and hypertension have been found to be highly correlated.[24] Considering these associations, it would seem natural that age and BMI were higher in the hypertensive group compared with that in the control group in our study. Hypertension also influences the ASA classification, and hypertensive patients tend to have other co-morbidities; thus, hypertensive patients would fall into a higher ASA class.

Glass et al.[25] reported that maintaining a BIS value below 50 is sufficient to eliminate recall and maintenance of adequate anesthetic depth. We adjusted the sevoflurane concentration to maintain a target BIS value of 40 to 50. In our study, the MAC value was lower than the MAC_{BIS50} value of 0.97% (range, 0.89%–1.05%) among middle-aged patients (41–69 years old), and similar results were also reported by Matsuura et al.[26] This difference is explained by the fact that in our study, midazolam was administered as premedication and remifentanil was administered concomitantly with sevoflurane. Opioids reduce the MAC when combined with inhaled anesthetics.[27–29] Because remifentanil is considered to reduce the MAC value, we attempted to adjust the concentration of sevoflurane targeting a BIS value of 40 to 50. Inhalational agents and propofol can also reduce blood pressure by decreasing the systemic vascular resistance and by causing myocardial depression. Propofol was administered based on the ideal body weight in all subjects, and there was no difference in the BIS and MAC values between the two groups. Therefore, it appears that the effect of vasodilation and cardiovascular depression resulting from inhalational anesthetic administration was similar in both groups.

Our study has several limitations. First, it is not a randomized controlled study. If we had further evaluated the hemodynamic response of normotensive and hypertensive patients without remifentanil administration, we would have been closer to a randomized controlled study. Second, we divided patients into two groups; it is possible that patients with undiagnosed

hypertension may have been assigned to the control group. We included patients in ASA class I or II, effectively excluding those with uncontrolled or undiagnosed hypertension. In future studies, untreated hypertensive patients could be grouped separately. Third, the effect-site concentration (concentration of drug at the site of its biological activity) of remifentanil cannot be measured accurately. Maruta et al.[13] calculated the effect-site concentrations of remifentanil based on a default formula from the electronic anesthesia record. We did not use a default program or a target-controlled infusion system; thus, it was not possible to estimate the effect-site concentration of remifentanil. The Minto formula[8] was used to calculate the effect-site concentration of remifentanil, and we confirmed that there was no difference between the two groups. Fourth, because the effect of remifentanil was observed after pretreatment with atropine, evaluation of the extent of the decrease in heart rate was limited. Compared with other studies that used a bolus administration, the rate of remifentanil administration in our study was slower; thus, the evaluation may have been more accurate if atropine pretreatment had been withheld. Fifth, in most studies, supplemental fluid was administered to prevent hypotension resulting from vasodilation and cardiac depression before the induction of anesthesia. However, we administered a relatively low volume of fluid (100 mL). The lower fluid volume may have affected the degree of blood pressure reduction compared with that in other studies. Finally, premedication with midazolam may have affected the BIS values. Therefore, the effect of remifentanil alone on the MAC could not be measured accurately.

In conclusion, a continuous infusion of remifentanil during the induction of general anesthesia resulted in a stable hemodynamic response in both hypertensive and normotensive patients.

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Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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Research ethics and patient consent

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