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Baroreflex sensitivity and hemodynamic changes in elderly and young patients during propofol anesthesia

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Introduction

Baroreflex is an important compensatory neural control system for maintaining cardiovascular stability. Increasing age has a significant impact on baroreflex sensitivity (BRS) [1]. Propofol is reported to be a potent inhibitor of sympathetic neural activity and to decrease BRS [2]. Thus, propofol anesthesia for elderly patients may markedly impair cardiovascular stability. However, BRS during propofol anesthesia in elderly patients has not been investigated.

Several studies have shown that propofol used for induction and maintenance of anesthesia decreases arterial blood pressure [3,4]. However, there were a few reports about age-related change in blood pressure during propofol anesthesia [5]. In addition, heart rate was reported to increase [3,4] or remain unchanged [6] during propofol anesthesia.

The objectives of the present study were, therefore, to investigate the influence of age on hemodynamics and BRS during propofol anesthesia, comparing elderly and young patients.

Methods

This study was approved by the Yamanashi Medical University Ethics Committee, and informed consent was obtained from all patients. Thirteen elderly patients, aged greater than 65 years (group E), and 13 young patients, aged 20–40 years (group Y) scheduled for elective surgery under general anesthesia participated in the present study. Patients with respiratory or cardiovascular disease, diabetes mellitus, or autonomic disorders, as well as patients receiving medication that affects cardiovascular function, were excluded. Premedication consisted of midazolam 0.05 mg·kg^{-1} administered intramuscularly 30 min before anesthesia. Monitors were placed to measure, noninvasively, blood pressure, continuous electrocardiography, and pulse oximetry. A venous catheter was inserted, and acetated Ringer's solution was infused at a rate of 10 ml·kg^{-1}·h^{-1}. After measurements of blood pressure and heart rate, all patients were anesthetized with a bolus propofol injection (1.5 mg·kg^{-1}), followed by continuous intravenous infusion (10 mg·kg^{-1}·h^{-1}). Vecuronium (0.15 mg·kg^{-1}) was given, and tracheal intubation was performed. Ten min after intubation, blood pressure and heart rate were re-evaluated. Then phenylephrine (2 μg·kg^{-1}) was injected. Blood pressure was measured by continuous mode, and heart rate was measured continuously for 10 min after the injection. Values for maximum increase in mean arterial blood pressure (ΔMAP) and maximum reflex decrease in heart rate (ΔHR) in response to phenylephrine-induced hypertension were obtained. The BRS was assessed as the ratio of ΔHR to ΔMAP (ΔHR/ΔMAP).

Patients' age, height, weight, and changes in blood pressure, changes in heart rate, and BRS were compared using unpaired *t*-test. Propofol-mediated changes in blood pressure and HR were analyzed by paired *t*-test. A P value less than 0.05 was considered statistically significant.

Results

There was an approximately 40-year age difference between groups E and Y ($P < 0.0001$). There were

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no significant differences in patients' heights or weights (Table 1).

After intravenous propofol infusion, the MAP was significantly decreased in both groups (group E, $P < 0.0001$; group Y, $P < 0.0005$), whereas there was no significant difference in HR (Table 2). The decrease in MAP was significantly greater in group E than in group Y ($P < 0.005$; Table 2).

Mean blood pressure before injection of phenylephrine was comparable in the two groups (Table 3). The responses of MAP to phenylephrine did not differ between groups E and Y (Table 3). Values for ΔHR induced by phenylephrine and BRS were significantly lower in group E than in group Y ($P < 0.05$; Table 3).

Discussion

Our results show that BRS, assessed by pressor tests with phenylephrine, is impaired in elderly patients as compared with young patients. In addition, propofol-induced hypotension was more prominent in elderly patients and was not accompanied by reflex tachycardia. Young patients also did not show reflex tachycardia in this study.

Aging may influence autonomic cardiovascular control mechanisms. The HR reflex response to alterations in arterial pressure was impaired with advancing age [7]. Furthermore, propofol has been shown to decrease the sensitivity of the baroreflex [2]. Because baroreflex is an important indicator of cardiac autonomic regulation, it is important to assess BRS during propofol anesthesia in elderly patients. Our results demonstrated that, under propofol anesthesia, BRS was suppressed more in the elderly group than in the young group. This may suggest that acute blood loss and hypotension during propofol anesthesia in elderly patients may result in greater cardiovascular instability due to the greater impairment of BRS.

The mechanism responsible for the impairment of BRS in elderly patients is still unclear. We used phenylephrine, given by bolus injection. In the study by Laitinen et al. [1], phenylephrine was administered as a bolus injection, and baroreflex was attenuated in elderly subjects. On the other hand, in the study by Davy et al. [8], phenylephrine was administered as graded continuous infusions, and arterial baroreflex was preserved in aged male subjects. Bolus injections of phenylephrine could have an acute and intense impact on the baroreflex control of sympathetic nerve activity and heart rate, and elderly subjects probably do not have time to adjust the integrity of the baroreflex mechanism. Methods of phenylephrine administration may be associated with impaired reflex bradycardia in elderly patients.

Other possibilities associated with such impaired reflex bradycardia may be age-related changes in arterial wall stiffness, peripheral nervous pathways, and central nervous control. The baroreceptor reflex responds to changes in blood pressure via circumferential and longitudinal stretch receptors [9]. Stretch response to blood pressure perturbation would be attenuated by arterial wall stiffness. Arterial wall compliance has been shown to be related to baroreceptor activation [10]. Increased

Table 1. Patient characteristics

	Age (years)	Height (cm)	Weight (kg)
Group E ($n = 13$)	74 ± 6*	155.4 ± 5.8	50.3 ± 6.8
Group Y ($n = 13$)	32 ± 5	160.4 ± 7.9	57.0 ± 11.7

Values are means ± SD or number of patients
Group E, Elderly group; group Y, young group
* $P < 0.0001$, compared with group Y

Table 2. Propofol-mediated changes in mean blood pressure and heart rate

	Before propofol	At 10 min of propofol	Changes
MAP (mmHg)			
Group E	97 ± 11	65 ± 9*	−32 ± 16***
Group Y	84 ± 7	69 ± 9**	−15 ± 10
HR (beat·min^{-1})			
Group E	75 ± 11	69 ± 15	−6 ± 12
Group Y	73 ± 8	72 ± 12	−1 ± 12

Values are means ± SD
MAP, Mean arterial blood pressure; HR, heart rate
* $P < 0.0001$; ** $P < 0.0005$ versus before propofol; *** $P < 0.005$ versus group Y

Table 3. Phenylephrine-induced increases in mean arterial blood pressure, decreases in heart rate, and baroreflex sensitivity

	MAP-Pre (mmHg)	MAP-Post (mmHg)	ΔMAP (mmHg)	HR-Pre (beat·min^{-1})	HR-Post (beat·min^{-1})	ΔHR (beat·min^{-1})	BRS (beat·min^{-1}·mmHg^{-1})
Group E	65 ± 9	85 ± 22	20 ± 16	69 ± 15	59 ± 16	−10 ± 8*	−0.6 ± 0.4*
Group Y	69 ± 9	94 ± 7	25 ± 11	72 ± 12	52 ± 9	−20 ± 6	−1.0 ± 0.6

Values are means ± SD
Group E, Elderly group; group Y, young group; MAP, mean arterial blood pressure; HR, heart rate; pre, before phenylephrine injection; post, after phenylephrine injection; ΔMAP, (MAP-Post)-(MAP-Pre); ΔHR, (HR-Post)-(HR-Pre); BRS, baroreflex sensitivity (ΔHR/ΔMAP)
* $P < 0.05$ versus group Y

arterial wall stiffness with aging may be involved in the impaired reflex bradycardia in elderly patients. In addition, increased blood pressure stimulates baroreceptors that send impulses along the glossopharyngeal nerve and vagal nerve to the medullary cardiovascular center. The responses are decreased sympathetic activity and increased parasympathetic activity that, in turn, decrease heart rate. Cardiac parasympathetic activity has been demonstrated to be progressively impaired with aging [11]. Reduced cardiac parasympathetic activity might also be responsible for the impairment of BRS.

In the present study, the propofol dose was identical in the elderly and the young patients. The same dose of propofol may produce more profound anesthesia in elderly than in young patients. The bispectral index (BIS) is a commercially available monitoring device, and its value correlates well with depth of sedation during propofol-induced hypnosis [12]. Baroreflex should be evaluated under comparable depth of sedation using BIS monitoring.

We observed that the decrease in blood pressure caused by propofol was greater in the elderly than in the young patients. Some studies have shown that propofol decreased sympathetic vasoconstrictor nerve activity [2,13]. Basal sympathetic nerve activity was suggested to be higher in elderly than in young subjects [11]. Blood pressure in the elderly may be maintained by increased basal sympathetic outflow. Therefore, a propofol-induced decrease in sympathetic nerve activity would cause greater reduction in blood pressure in elderly patients than in young patients.

Although the MAP significantly decreased after the induction of anesthesia with propofol, the HR did not change in either group. It has been shown that baroreflex-mediated tachycardia in response to arterial hypotension is attenuated during propofol anesthesia [14]. In addition, propofol produces vagal predominance of HR control by reducing sympathetic tone to a greater extent than parasympathetic tone [6]. Propofol-induced hypotension without reflex tachycardia might be caused by impaired baroreflex and reduced sympathetic tone under propofol anesthesia.

In conclusion, age has a significant impact on the BRS and reflex bradycardia elicited by phenylephrine during propofol anesthesia. Propofol-induced hypotension is more prominent in elderly patients and is not accompanied by reflex tachycardia.

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