Surgical stress attenuates reflex heart rate response to hypotension

Naoko Kohno MD,
Chikuni Taneyama MD

Purpose: The baroreflex-mediated increase in heart rate (HR) in response to acute reduction of systolic blood pressure (SBP) was studied in order to assess whether the changes in arterial baroreflex sensitivity depend on the intensity of surgical stress, and location of visceral and somatic stimulation during surgery.

Methods: Patients were divided into visceral stimulation groups [upper ($n = 30$) and lower ($n = 30$) abdominal surgery] and somatic stimulation groups [upper ($n = 25$) and lower ($n = 25$) limbs, and chest wall ($n = 25$) surgery]. Acute hypotension as a baroreflex depressor test was induced by prostaglandin E_1 (PGE_1) 10 min before surgical incision (control) and during surgical manipulation under isoflurane- N_2O anaesthesia or isoflurane- N_2O -fentanyl anaesthesia. Plasma level of ACTH was measured in an additional 40 patients who underwent upper abdominal surgery.

Results: During upper abdominal surgery, the heart rate baroreflex sensitivity ($\Delta HR/\Delta SBP$) was depressed from -0.47 ± 0.05 (control) to -0.01 ± 0.04 ($P < 0.05$). The reflex heart rate baroreflex sensitivity remained unchanged and was similar among the remaining groups of patients. The concentration of ACTH increased from 12.5 ± 1.0 (control) to 343 ± 78.6 $pg \cdot ml^{-1}$ ($P < 0.05$) with isoflurane- N_2O anaesthesia but did not change with isoflurane- N_2O -fentanyl anaesthesia during upper abdominal surgery.

Conclusion: Upper abdominal surgery is associated with the most stressful stimulation to attenuate heart rate baroreflex sensitivity. Integrity of the baroreflex can be preserved by adding opioids to supplement inhalation anaesthesia.

Objectif : L'augmentation de la fréquence cardiaque (FC) à médiation baroréflexe en réponse à une diminution soudaine de la tension artérielle systolique (TAS) a été étudiée dans le but d'évaluer si les changements de sensibilité artérielle baroréflexe dépendent de l'intensité du stress chirurgical et du siège de la stimulation viscérale et somatique pendant la chirurgie.

Méthode : Les patients ont été répartis en différents groupes : selon une stimulation viscérale [chirurgie abdominale haute ($n = 30$) et basse ($n = 30$)] et selon une stimulation somatique [chirurgie des membres supérieurs ($n = 25$) et inférieurs ($n = 25$) ou chirurgie de la paroi thoracique ($n = 25$)]. Une hypotension soudaine, sous forme de test déresseur baroréflexe, a été induite par la prostaglandine E_1 (PGE_1) 10 min avant l'incision chirurgicale (groupe témoin) et pendant la manipulation chirurgicale sous anesthésie avec isoflurane N_2O ou sous anesthésie avec isoflurane N_2O et fentanyl. Le niveau plasmatique d'ACTH a été mesuré chez 40 patients additionnels admis pour une chirurgie abdominale haute.

Résultats : Pendant la chirurgie abdominale haute, la sensibilité de la fréquence cardiaque baroréflexe ($\Delta FC / \Delta TAS$) était abaissée de $-0,47 \pm 0,05$ (témoin) à $-0,01 \pm 0,04$ ($P < 0,05$). La sensibilité réflexe de la fréquence cardiaque baroréflexe n'a pas changé et était similaire parmi les autres groupes de patients. La concentration d'ACTH a augmenté de $12,5 \pm 1,0$ (témoin) à $343 \pm 78,6$ $pg \cdot ml^{-1}$ ($P < 0,05$) avec l'anesthésie à l'isoflurane N_2O mais n'a pas changé avec l'anesthésie à l'isoflurane N_2O et au fentanyl pendant la chirurgie abdominale haute.

Conclusion : La chirurgie abdominale haute est associée à la stimulation la plus stressante pour atténuer la sensibilité de la fréquence cardiaque baroréflexe. L'intégrité du baroréflexe peut être préservée en ajoutant des opioïdes pour compléter l'anesthésie par inhalation.

From the Department of Anesthesiology, Suwa Red Cross Hospital, Suwa Nagano, and Shinshu University School of Medicine, Matsumoto Nagano 390 Japan.

Address correspondence to: Chikuni Taneyama MD, Division of Anesthesiology and Pain Clinic, Taneyama Clinic, 5-6-28 Daimon, Shiojiri City, 399-0732 Nagano, Japan. Phone: 81-0263-53-1010; Fax: 81-0263-52-1363; E-mail: taneyai@avisnet.or.jp

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GENERAL anaesthetics depress arterial baroreflex control of heart rate in humans and animals.¹⁻³ Noxious surgical stimuli not only stimulate the autonomic nervous system but may change the integrity of various autonomic responses, including baroreflex-mediated heart rate responsiveness during general anaesthesia.⁴ Within the context of interaction of general anaesthesia and noxious surgical stimuli, the question of how baroreflex integrity changes during different locations of surgery arises. We hypothesized that surgical stress can affect the arterial baroreflex, depending on the intensity and location of visceral and somatic stimulation, during surgery. In this study, we examined whether the reflex heart rate response to acute hypotension is affected by different locations of visceral and somatic surgical stimulation, and whether impaired reflex heart rate responsiveness can be alleviated by reducing the intensity of surgical stimulation by adding opioids to general anaesthesia.

Methods

Informed consent was obtained from all patients, and the study was approved by the Hospital Clinical Trial Committee. One hundred and seventy five ASA I-II patients scheduled to receive general endotracheal anaesthesia were studied. We excluded patients with any history of cardiopulmonary or neurological disorders and diabetes mellitus, and those receiving medication which might affect the cardiovascular and nervous systems.

Preoperative medication consisted of 0.5 mg atropine sulfate and 30 mg pentazosine *im* one hour before induction of anaesthesia. Anaesthesia was induced gradually with isoflurane 0.5 - 2% in oxygen via a face mask, and tracheal intubation was facilitated with 0.15 mg·kg⁻¹ vecuronium. In all patients the lungs were mechanically ventilated with nitrous oxide and isoflurane in oxygen (F_IO₂ 0.35), with a tidal volume of 10-

12 ml·kg⁻¹ and a respiratory rate of 10-12 bpm.

End-tidal concentrations of CO₂ (ETCO₂) and isoflurane (ETIso), and haemoglobin oxygen saturation (SpO₂) were continuously measured using a Capnomac Ultima (Datex, Helsinki, Finland). The ETIso was maintained at 0.4 to 0.5% until surgical incision and at about 1% during surgery in all patients. The ECG (lead II) was recorded for electronic calculation of heart rate, and systolic arterial blood pressure (SBP) was measured with Finapress⁵ (Finapress Ohmeda, Louisville, CO). Lactated Ringer's solution was infused intravenously at a rate of 10 ml·kg⁻¹·hr⁻¹.

The first part of the study was designed to evaluate the relationship between heart rate baroreflex sensitivity to acute hypotension and the location of surgical stimulation. One hundred and thirty-five patients were divided into two groups: visceral stimulation and somatic stimulation groups. Visceral stimulation groups consisted of two subgroups: patients undergoing upper abdominal (gastrointestinal, n = 30) and lower abdominal (gynaecological and urological, n = 30) surgery. Somatic stimulation groups consisted of three subgroups: patients undergoing upper (n = 25) and lower (n = 25) limb orthopaedic surgery, and chest wall (mastectomy and plastic, n = 25) surgery.

Depressor tests to measure reflex heart rate response to acute hypotension were carried out approximately 10 min before and 30-40 min after surgical incision. Acute arterial hypotension was induced with PGE₁ after at least five minutes of haemodynamic stability. Following a bolus injection of 0.007 µg·kg⁻¹, PGE₁ was infused at a rate of 0.1-0.3 µg·kg⁻¹·min⁻¹ for five minutes. This dose sequence was found to reduce arterial blood pressure by 20-25 mmHg in a preliminary study.⁶ Prior to and during the injection of PGE₁, the inspired concentration of isoflurane was kept constant for at least 15 min. Heart rate baroreflex sensitivity to acute hypoten-

TABLE I ETIso, ETCO₂ and SpO₂ immediately before each depressor test

		ETIso (%)	ETCO ₂ (mmHg)	SPO ₂ (%)
upper abdominal (n = 30)	before surgical incision	0.43 ± 0.02	34.4 ± 0.7	98.5 ± 0.2
	during surgery	0.98 ± 0.06*	36.5 ± 0.5	98.6 ± 0.2
lower abdominal (n = 30)	before surgical incision	0.45 ± 0.02	33.6 ± 0.7	98.9 ± 0.2
	during surgery	1.10 ± 0.09*	32.7 ± 0.7	98.7 ± 0.2
upper limbs (n = 25)	before surgical incision	0.48 ± 0.05	35.3 ± 0.7	98.6 ± 0.3
	during surgery	1.00 ± 0.06*	34.5 ± 0.7	98.4 ± 0.3
lower limbs (n = 25)	before surgical incision	0.44 ± 0.01	34.5 ± 0.7	98.7 ± 0.2
	during surgery	0.99 ± 0.07*	35.1 ± 0.6	98.5 ± 0.2
chest wall (n = 25)	before surgical incision	0.45 ± 0.01	34.9 ± 0.7	98.8 ± 0.2
	during surgery	0.94 ± 0.05*	34.4 ± 0.7	98.8 ± 0.2

Values are mean ± SE. ETIso: end-tidal isoflurane concentration. ETCO₂: end-tidal CO₂. SpO₂: haemoglobin oxygen saturation

* : P < 0.05 compared with values before surgical incision

TABLE II SBP, HR and delta changes (Δ SBP, Δ HR) during depressor tests

		SBP (mmHg)		Δ SBP (mmHg)	HR (bpm)		Δ HR (bpm)
		baseline	after infusion		baseline	after infusion	
upper abdominal (n = 30)	before surgical incision	105.3 $\pm$ 1.9	81.2 $\pm$ 2.2	-22.9 $\pm$ 1.4	76.2 $\pm$ 2.2	85.6 $\pm$ 2.3	+9.4 $\pm$ 0.5
	during surgery	137.2 $\pm$ 3.6*†	112.5 $\pm$ 3.2	-24.7 $\pm$ 2.2	94.4 $\pm$ 2.9*†	97.1 $\pm$ 3.0	+2.7 $\pm$ 0.7*†
lower abdominal (n = 30)	before surgical incision	103.5 $\pm$ 2.4	82.6 $\pm$ 2.9	-22.8 $\pm$ 1.8	73.2 $\pm$ 2.3	81.8 $\pm$ 2.7	+7.9 $\pm$ 0.8
	during surgery	128.1 $\pm$ 3.8*	107.5 $\pm$ 3.62	-22.6 $\pm$ 1.4	82.2 $\pm$ 3.0*	90.3 $\pm$ 3.2	+8.1 $\pm$ 0.9
upper limbs (n = 25)	before surgical incision	101.2 $\pm$ 2.5	77.2 $\pm$ 3.6	-24.6 $\pm$ 3.1	79.6 $\pm$ 2.5	90.8 $\pm$ 2.3	+11.2 $\pm$ 1.4
	during surgery	128.4 $\pm$ 3.2*	102.2 $\pm$ 3.8	-26.3 $\pm$ 1.9	85.7 $\pm$ 2.8*	97.3 $\pm$ 3.0	+11.5 $\pm$ 1.1
lower limbs (n = 25)	before surgical incision	106.4 $\pm$ 3.3	82.2 $\pm$ 3.1	-24.2 $\pm$ 2.3	75.3 $\pm$ 2.6	86.7 $\pm$ 3.0	+10.5 $\pm$ 1.1
	during surgery	126.8 $\pm$ 4.2*	99.4 $\pm$ 4.0	-25.4 $\pm$ 2.1	84.8 $\pm$ 3.5*	95.2 $\pm$ 3.8	+10.4 $\pm$ 1.2
chest wall (n = 25)	before surgical incision	102.5 $\pm$ 2.7	77.6 $\pm$ 3.1	-24.9 $\pm$ 1.8	79.1 $\pm$ 3.0	88.2 $\pm$ 3.3	+9.9 $\pm$ 0.8
	during surgery	128.9 $\pm$ 3.3*	102.8 $\pm$ 2.9	-25.1 $\pm$ 2.1	89.5 $\pm$ 2.7*	99.7 $\pm$ 2.4	+10.1 $\pm$ 0.9

Values are mean $\pm$ SE. SBP: systolic blood pressure. HR: heart rate

* : $P < 0.05$ compared with values before surgical incision. † : $P < 0.05$ compared with corresponding values in other surgical groups

TABLE III SBP, HR and delta changes (Δ SBP, Δ HR) during depressor tests. (Isoflurane - N₂O vs Isoflurane-N₂O-Fentanyl anaesthesia during upper abdominal surgery)

		SBP (mmHg)		Δ SBP (mmHg)	HR (bpm)		Δ HR (bpm)
		baseline	after infusion		baseline	after infusion	
Isoflurane-N ₂ O (n = 20)	before surgical incision	105.7 $\pm$ 1.7	80.7 $\pm$ 1.9	-25.1 $\pm$ 1.4	80.7 $\pm$ 1.9	88.5 $\pm$ 2.0	+8.9 $\pm$ 0.5
	during surgery	138.5 $\pm$ 3.2*†	113.1 $\pm$ 2.8	-25.4 $\pm$ 1.8	91.9 $\pm$ 2.6*†	94.1 $\pm$ 2.6	+2.3 $\pm$ 0.5*†
Isoflurane-N ₂ O-Fentanyl (n = 20)	before surgical incision	108.0 $\pm$ 2.6	77.8 $\pm$ 2.9	-27.2 $\pm$ 1.8	64.9 $\pm$ 1.6	74.0 $\pm$ 1.9	+9.1 $\pm$ 0.7
	during surgery	117.1 $\pm$ 2.3*	89.9 $\pm$ 2.3	-26.1 $\pm$ 1.8	74.7 $\pm$ 2.1 *	82.4 $\pm$ 2.2	+7.8 $\pm$ 0.6

Values are mean $\pm$ SE.

See table II for abbreviation

* : $P < 0.05$ compared with values before surgical incision

† : $P < 0.05$ compared with corresponding values in isoflurane-N₂O-fentanyl group

sion was assessed, using the ratio of maximal increase of heart rate to maximal reduction of systolic blood pressure (Δ HR/ Δ SBP).⁷

Blood pressure and heart rate were recorded continuously on digital audio tape (CT90 type II TEAC R60 Tokyo, Japan) and analyzed for Δ HR/ Δ SBP by Vitalism NO9801 (NEC San-ei, Tokyo, Japan).

The second part of the study was designed to determine whether attenuated reflex heart rate responsiveness during upper abdominal surgery can be alleviated by adding fentanyl to general anaesthesia, thus reducing the intensity of surgical stimulation.

An additional 40 patients who underwent upper abdominal surgery were divided into two groups; isoflurane-N₂O (GOI) Group and isoflurane-N₂O-fentanyl anaesthesia (GOI-F) Group. In the GOI-F group, fentanyl was initially injected at 20 μ g·kg⁻¹ before surgical incision, followed by an intravenous infusion of 2 μ g·kg⁻¹·hr⁻¹ during surgery. Otherwise, induction and maintenance of anaesthesia were the

same as in the first part of the study. In the second part of the study, arterial blood samples were withdrawn for measurement of plasma ACTH concentrations just before each depressor test. The ACTH concentration was determined using ACTH radio-immunoassay kits.

All data were expressed as mean $\pm$ SE. Statistical analyses were performed using repeated measures two-way ANOVA followed by Scheffe's test. Differences with a statistical probability of less than 0.05 were considered significant.

Results

In the first part of the study, there were no characteristic differences among groups: upper abdominal surgery (n = 30, 47.4 $\pm$ 2.1 yr, BW 54.3 $\pm$ 3.2 Kg), lower abdominal surgery (n = 30, 47.0 $\pm$ 2.2 yr, BW 55.1 $\pm$ 2.4 Kg), upper limbs (n = 25; 47.0 $\pm$ 4.4 yr, BW 52.7 $\pm$ 3.2 Kg), lower limbs (n = 25; 44.8 $\pm$ 4.8 yr, BW 53.8 $\pm$ 6.1 Kg), and chest wall (n = 25; 52.3 $\pm$ 2.7 yr, BW 54.3 $\pm$ 2.8 Kg).

The values of ET_{CO}₂ and SpO₂ prior to each

FIGURE 1 The reflex heart rate response to acute hypotension ($\Delta\text{HR}/\Delta\text{SBP}$) before surgical incision and during surgery under isoflurane- N_2O anaesthesia. Note that $\Delta\text{HR}/\Delta\text{SBP}$ was depressed during upper abdominal surgery.

FIGURE 2 The reflex heart rate response to acute hypotension ($\Delta\text{HR}/\Delta\text{SBP}$) before surgical incision and during upper abdominal surgery under isoflurane- N_2O (GOI Group) and isoflurane- N_2O -fentanyl anaesthesia (GOI-F Group). $\Delta\text{HR}/\Delta\text{SBP}$ in the GOI group was suppressed during surgery.

depressor test were all within normal limits and were not different among groups (Table I). End-tidal isoflurane concentrations (ETIso) were higher ($P < 0.05$) during surgery in all groups, but were not different among groups before surgical incision and during surgery (Table I). The SBP and HR increased ($P < 0.05$) despite increased ETIso during surgery in all groups (Table II). However, the degree of increased SBP and HR in upper abdominal surgery were greater

FIGURE 3 The changes in plasma ACTH concentration before surgical incision and during upper abdominal surgery in the GOI and GOI-F groups. The plasma ACTH concentration increased in the GOI group during surgery, but remained unchanged in the GOI-F group.

than those in the remaining groups. The SBP was reduced to the same extent by PGE1 in all groups both before and after surgical incision. In the presence of surgical stimulation, ΔHR was smaller in the upper abdominal surgery group ($P < 0.05$).

Figure 1 shows the heart rate baroreflex sensitivity ($\Delta\text{HR}/\Delta\text{SBP}$) before surgical incision and during surgery in all groups. During upper abdominal surgery, $\Delta\text{HR}/\Delta\text{SBP}$ was depressed from -0.47 ± 0.05 to -0.11 ± 0.04 bpm/mmHg, but it remained unchanged in other surgery groups.

In the second part of the study, there were also no demographic differences between the GOI ($n = 20$, 51.3 ± 2.0 yr, BW 56.1 ± 2.1 Kg) and GOI-F groups ($n = 20$, 52.4 ± 1.1 yr, BW 55.8 ± 1.8 Kg). The ETIso(%), ETCO_2 (mmHg) and SpO_2 (%) were consistent with the first part of the study.

The SBP and HR in the GOI group increased compared with those in the GOI-F groups, and the delta HR during surgery was smaller in the GOI group (Table III).

Figure 2 shows the $\Delta\text{HR}/\Delta\text{SBP}$ before surgical incision and during upper abdominal surgery in the two anaesthesia groups. In the GOI group, $\Delta\text{HR}/\Delta\text{SBP}$ was depressed from -0.42 ± 0.04 to -0.09 ± 0.03 bpm/mmHg during surgery, while it remained unchanged in the GOI-F group. The plasma ACTH concentration increased from 12.5 ± 1.6 , pre-incision to 343 ± 78.6 pg·ml⁻¹ during surgical stimulation in

the GOI group. ($P < 0.05$), but did not increase in the GOI-F group (Figure 3).

Discussion

Most general anaesthetics depress arterial baroreflex control of heart rate in humans.^{2,3} However, noxious surgical stimuli increase adrenergic activity and may counteract the depressant effect of general anaesthetics on baroreflex integrity.^{4,8} Takeshima and Dohi speculated that baroreflex sensitivity may increase due to noxious surgical stimulation because it remained unchanged even though higher levels of isoflurane were required during surgery.⁹ Latson *et al.* showed that noxious surgical stimulation can reverse the depressant effects of anaesthetics on autonomic reflex function.¹⁰ The results in our study generally agreed with their findings: Heart rate baroreflex sensitivity remained unchanged during surgery except in upper abdominal surgery, even though concentrations of isoflurane were increased. Because the MAC value of isoflurane in N₂O 70% is 0.5%, end-tidal concentrations of isoflurane were maintained at approximately 0.4 to 0.5% before surgical incision, and at approximately 1% during surgical manipulation in all patients (Table II).

The degree of noxious surgical stimulation seems to be similar in all patients except those who underwent upper abdominal surgery, since arterial blood pressure and heart rate increased to the same extent during surgical manipulation (Table II). On the other hand, blood pressure and heart rate during surgical manipulation were higher in the upper abdominal surgery group than in the other surgical groups, in spite of similar concentrations of end-tidal isoflurane (Table II). This indicates that upper abdominal surgery is associated with more intense stimuli and/or different kinds of stimuli than surgery in other areas, and heart rate baroreflex sensitivity was decreased during upper abdominal surgery.

Noxious surgical stimuli cause both somatic and visceral pain and can produce different physiological reactions in the autonomic nervous and the endocrine systems.¹¹⁻¹³ It has been shown that the hypothalamic-adrenocortical responses (increases in ACTH and cortisol) during lower abdominal surgery are similar to operations which involve somatic stimuli, and are suppressed by somatic nerve block or thoraco-lumbar epidural blocks.¹³⁻¹⁴ Increases in such stress hormones, however, cannot effectively be suppressed even by high epidural anaesthesia during upper abdominal surgery,^{15,16} but they are suppressed by epidural blocks combined with splanchnic nerve block.¹⁷ Upper abdominal surgery inevitably stimulates the coeliac plexus and the splanchnic nerves, and visceral stress via

splanchnic afferents may elicit different physiological consequences compared with the stress from surgery on other parts of the body. Nosaka *et al.*¹⁸ showed that splanchnic nerve stimulation causes suppression of the arterial baroreflex, and it has been shown that autonomic responses, arterial baroreflex in particular, are suppressed by stimulation of the defence area of the hypothalamus.^{4,19} Furthermore, ACTH, secreted by the hypothalamus, is found to suppress baroreflex control of heart rate.²⁰ It is speculated, therefore, that the noxious visceral stimuli transmitted via the coeliac plexus and splanchnic efferents might have intensely stimulated the hypothalamus, resulting in attenuated reflex heart rate responsiveness during upper abdominal surgery in our study.

The question is raised whether increased blood pressure and heart rate per se during upper abdominal surgery contributed to the decreased heart rate baroreflex responsiveness. In the remainder of surgical groups, baseline heart rate and systolic blood pressure increased from their pre-incision baseline values, yet ΔHR and heart rate baroreflex sensitivity ($\Delta HR/\Delta SBP$) remained the same. This suggests that, although the baroreflex sigmoid curve relationship between blood pressure and heart rate has shifted due to increased sympathetic activity secondary to surgical stimulation, the steepness of the straight portion of the sigmoid curve remains unchanged, and new set points are not on the flat portion of the sigmoid curve. On the other hand, general anaesthetics can shift the baroreflex sigmoid curve in the opposite direction to sympathetic overactivity when both blood pressure and heart rate decrease together. The results from the study in dogs by Seagard *et al.*¹ indicated that the new set points are close to the midpoints of the straight portion of the shifted baroreflex curve, even though both blood pressure and heart rate were markedly decreased by isoflurane. Therefore, we believe that shifted baroreflex set points after increased blood pressure and heart rate during upper abdominal surgery were close to the midpoint of the straight portion of the shifted sigmoid curve, and decreased $\Delta HR/\Delta SBP$ (Figures 1, 2) truly indicated the attenuated heart rate baroreflex sensitivity.

Fentanyl has been used to provide haemodynamic stability and stress-free anaesthesia;^{21,22} however, the effect of fentanyl on arterial baroreflex has been controversial.^{2,23} We reported that the effect of fentanyl on arterial baroreflex control of sympathetic nerve activity in dogs was negligible.²⁴ The current study also indicates this, since $\Delta HR/\Delta SBP$ was similar under the isoflurane-N₂O anaesthesia with and without fentanyl before surgical stimulation (Figure 2). In the presence of surgical stimulation, however, fentanyl preserved heart rate baroreflex

sensitivity (Figure 2) and prevented an increase in ACTH (Figure 3), presumably by suppressing visceral surgical noxious stimuli during upper abdominal surgery.

It is debatable whether preservation of the arterial baroreflex during surgery is beneficial to patients. If arterial baroreflex integrity is preserved, the patient can compensate for acute and massive blood loss by increasing heart rate and systemic peripheral resistance. Thus, there is time to start blood transfusion before patients decompensate. On the other hand, hidden blood loss may be overlooked since blood pressure does not decrease with well preserved arterial baroreflex integrity. Nevertheless, we believe that preserved arterial baroreflex is important during surgery since acute and massive blood loss obviously implies urgent impact to the patient's haemodynamics.

All patients received atropine *im* (routine in Japan) one hour prior to induction of anaesthesia. The parasympatholytic effect of atropine on the heart rate response, if any, should not have differed between the first and second baroreflex depressor tests. This is because the duration of action of atropine is fairly long and the time between the two depressor tests was only approximately 40-50 min. It should be mentioned that increased heart rate in response to induced arterial hypotension is due not only to a reflex increase in efferent sympathetic activity but also to a depressed parasympathetic nervous system. Even though patients received *im* atropine premedication, fentanyl, a central vagotonic agent, decreased baseline heart rate before surgical incision (Table III). This suggests that atropine was not exerting full vagolytic action in our patients. We used only depressor tests with PGE₁ to evaluate heart rate baroreflex sensitivity since arterial baroreflex may respond more actively to a decrease in pressure than to an increase.²⁵ The assessment of cardiac baroreflex sensitivity to reduction of blood pressure has been examined using nitroglycerin (NTG).²⁶ In the present study, however, we chose prostaglandin E₁ as a depressor, since PGE₁ acts primarily on the arterial system and produces steady levels of hypotension even under surgical stress.

In summary, somatic stress during upper and lower limb and chest wall surgery, and visceral stress during lower abdominal surgery did not affect baroreflex control of heart rate under isoflurane-N₂O anaesthesia. This is probably because these stimuli were not strong enough to elicit larger stress responses. Instead, they might have counteracted the depressant effect of isoflurane on heart rate baroreflex sensitivity by increasing adrenergic activity. Baroreflex control of heart rate was attenuated during isoflurane-N₂O anaesthesia without supplemental fentanyl during upper abdominal surgery in which the

splanchnic nerves via the coeliac plexus are stimulated. On the other hand, the lower hypogastric plexus is most likely involved in noxious visceral stimuli during lower abdominal surgery. There may be quantitative and/or qualitative differences in visceral surgical stress between upper and lower abdominal surgery. Our data suggest that high-dose fentanyl is indicated to supplement general anaesthetics, particularly for upper abdominal surgery, to preserve arterial baroreflex integrity.

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