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Site of fresh gas inlet and ratios of the delivered fraction and inspired fraction of inhaled isoflurane and sevoflurane in low-flow anesthesia

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Abstract
Purpose. The use of low-flow anesthesia causes a discrepancy between the delivered fraction (FD) and the inspired fraction (FI) of inhaled gases. We compared the FI/FD ratios of a new circle (fresh gas inlet located between the inspiratory valve and the patient) to those of the conventional circle (fresh gas inlet located between the inspiratory valve and the CO_2 absorber) in low-flow isoflurane and sevoflurane anesthesia, using three anesthetic machines (Dräger NM-GS, Dräger Fabius-GS, and ACOMA KMA-1300-III).
Methods. Eighty-two patients were randomly assigned to three experimental groups. For experiment 1, 32 patients were allocated to the NM-GS conventional/new, NM-GS new/conventional, ACOMA conventional/new, and ACOMA new/conventional groups. For experiment 2, 14 patients were allocated to ACOMA conventional/conventional and ACOMA new/new groups to measure isoflurane FI/FD ratios. For experiment 3, 36 patients were allocated to ACOMA conventional/conventional, ACOMA new/new, Fabius conventional/conventional, and Fabius new/new to measure sevoflurane FI/FD ratios.
Results. In experiment 1, the NM-GS showed no significant changes in the FI/FD ratios. However, in the ACOMA, the new circle improved the FI/FD ratio. In experiment 2, the isoflurane FI/FD ratios in the new circle of the ACOMA were significantly higher than those in the conventional circle. In experiment 3, the sevoflurane FI/FD ratios in the new circle of both the ACOMA and the Fabius were significantly higher than those in the conventional circles.
Conclusion. The positioning of the fresh gas inlet between the inspiratory valve and the patient improved the FI/FD ratios of both isoflurane and sevoflurane during low-flow anesthesia in two decoupling-style anesthetic machines (ACOMA and Fabius).

Key words Anesthetic machine · Fresh gas inlet · Low-flow anesthesia · FI/FD ratio · Isoflurane · Sevoflurane

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Introduction

The use of low-flow anesthesia has become increasingly popular, because it is economical and reduces atmospheric pollution [1,2]. However, this type of anesthesia causes a discrepancy between the delivered fraction (FD) and the inspired fraction (FI) of inhaled gases, which might impair the ability to control acute hemodynamic responses to noxious surgical stimulation.

The basic arrangements of the modern semiclosed circle were established by Eger and Ethans [3]. The placement of the inflow, outflow, and two unidirectional valves was considered for the prevention of both CO_2 rebreathing and the waste of anesthetic gases. The resultant design may be economically optimal during high-flow anesthesia, but not during low-flow anesthesia. During high-flow fresh gas anesthesia, it is important to keep the fresh gas inlet at a distance from the adjustable pressure limiting (APL) valve to prevent the waste of volatile anesthetic gases. Changing the location of the fresh gas inlet to be closer to the APL valve may not incur too great a disadvantage for low-flow anesthesia.

In the present study, we changed the location of the fresh gas inlet to improve the control of inhaled gas concentrations in low-flow anesthesia. We compared the isoflurane and sevoflurane FI/FD ratios in our new circle (fresh gas inlet placed between the inspiratory valve and the patient) to those in the conventional circle (fresh gas inlet placed between the inspiratory valve and CO_2 absorber) in low-flow aesthesia ($11 \cdot min^{-1}$), using three anesthetic machines (Dräger NM-GS and Dräger Fabius-GS; Lübeck, Germany, and ACOMA KMA-1300-III; Tokyo, Japan).

Patients and methods

The University of Tsukuba Ethics Committee approved the study, and written informed consent was obtained

from all patients. We studied 82 patients classified as American Society of Anesthiologists (ASA) physical status I and II scheduled for elective surgery under general anesthesia, with or without epidural anesthesia and with an anticipated anesthesia time of 2.5-h duration or greater. Patients who had a history of or laboratory or physical evidence of hepatic, renal, or significant cardiovascular disease were excluded from the study.

Experiment 1: assessment of circle changing (isoflurane)

Thirty-two patients were randomly assigned to one of two anesthetic machine groups (Dräger NM-GS and ACOMA KMA-1300-III). Each group was randomly subdivided into conventional/new (C/N) and new/conventional (N/C) groups.

Experiment 2: 2-h evaluation (isoflurane)

Fourteen patients were randomly divided into ACOMA conventional/conventional (C/C) and ACOMA new/new (N/N) groups.

Experiment 3: 2-h evaluation (sevoflurane)

Thirty-six patients were randomly divided into ACOMA conventional/conventional (C/C), ACOMA new/new (N/N), Dräger Fabius conventional/conventional (C/C), and Dräger Fabius new/new (N/N) groups.

Methods

For all experimental groups patients were premedicated with diazepam 2–10 mg orally 90 min before arriving in the operating room. Anesthesia was induced with thiamylal sodium 5 mg·kg^{-1} and fentanyl 1–2 mg·kg^{-1}. Intubation was facilitated by vecuronium 0.2 mg·kg^{-1}. Anesthesia was maintained with 1% isoflurane or 2% sevoflurane in 50% oxygen and fentanyl and/or epidural anesthesia. Fresh gas flow was supplied to the circle system at 6 l·min^{-1} (2.4 l·min^{-1} oxygen and 3.6 l·min^{-1} air) during the first 20 min and then adjusted to 1 l·min^{-1} with an isoflurane vaporizer setting of 1% or with a sevoflurane vaporizer setting of 2%. The fresh gas outlet, fresh gas inlet, and proximal site of the inspiratory limb were connected by three tubes and a t-type connector. Schematic diagrams of the conventional and new circles are shown in Fig. 1. We changed the location of the fresh gas inlet from conventional to new, or vice versa, using the t-type connector, in the first half (60 min) of low-flow anesthesia in experiment 1. After a 120-min observation period, fresh gas flow was returned to 2 l·min^{-1} (10 min) and 6 l·min^{-1} (10 min) to confirm the vaporizer setting (1% or 2%). Isoflurane and

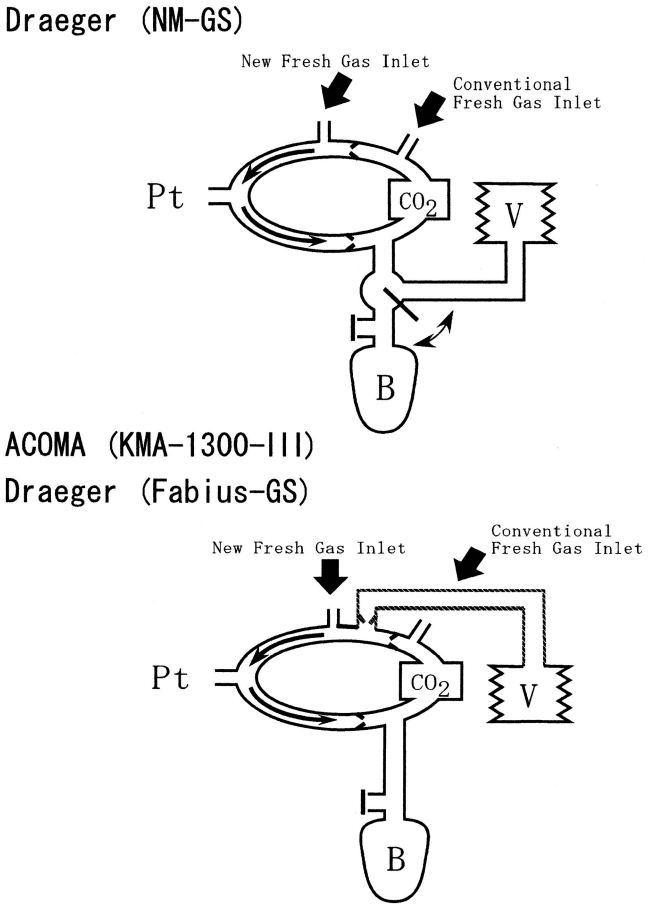

Fig. 1. Schematic diagrams of the Dräger NM-GS (*upper*), ACOMA KMA-1300-III (*lower*), and Dräger Fabius-GS (*lower*) anesthetic machines. *Pt*, patient site; *V*, ventilator; *B*, reservoir bag; *CO_2*, CO_2 absorber

sevoflurane concentrations were measured using the Datex AS/3 device (Division of Instrumentarium, Helsinki, Finland). The tidal volume and ventilator rate were set 8–10 ml·kg^{-1} and 8–10 breaths·min^{-1}, respectively, to maintain mild hypocapnia (34–36 mmHg). During the procedure, electrocardiogram (ECG; lead II), heart rate (HR), noninvasive blood pressure (NIBP), oxygen saturation (S_{PO_2}), body temperature, and bispectral (BIS) sensor (Aspect Medical Systems, Newton, MA, USA) data were monitored routinely. The inspired and end-tidal concentrations of oxygen, CO_2, and isoflurane or sevoflurane were recorded at 10-min intervals throughout the study.

All data are reported as mean values with variability expressed as SD. We used one-way analysis of variance and the χ^2 test with Yates' correction for demographic data. The inspired concentrations of isoflurane or sevoflurane were analyzed with the paired *t*-test or unpaired *t*-test. *P* values of less than 0.05 were considered statistically significant. The sample size of experiment 2 was based on the results of experiment 1, i.e., a two-

Table 1. Demographic data of patients in experiment 1

	Machine			
	Dräger NM-GS		ACOMA KMA-1300-III	
Group	C/N	N/C	C/N	N/C
n	9	7	9	7
Age (years)	60 ± 18	58 ± 13	59 ± 12	62 ± 13
Sex (M/F)	4/5	1/6	4/5	5/2
Height (cm)	158 ± 8	156 ± 11	158 ± 9	158 ± 7
Weight (kg)	55 ± 11	50 ± 9	61 ± 9	57 ± 10
BMI (kg/m^2)	22 ± 4	20 ± 1	25 ± 4	23 ± 3

Values are means ± SD
C/N and N/C, conventional/new group and new/conventional group, respectively; BMI, body mass index

Table 2. Effects of the changed circle on the FI/FD ratio in experiment 1

	min						
	60	70	80	90	100	110	120
Dräger NM-GS							
C/N	0.77	0.77	0.78	0.78	0.78	0.78	0.78
	(0.08)	(0.06)	(0.07)	(0.07)	(0.07)	(0.07)	(0.07)
N/C	0.76	0.78	0.79	0.79	0.79	0.79	0.79
	(0.03)	(0.05)	(0.05)	(0.06)	(0.06)	(0.07)	(0.06)
ACOMA KMA-1300-III							
C/N	0.61	0.65*	0.66*	0.65*	0.65*	0.65*	0.65*
	(0.04)	(0.03)	(0.03)	(0.03)	(0.03)	(0.02)	(0.03)
N/C	0.65	0.59*	0.6*	0.61*	0.61*	0.61*	0.61*
	(0.03)	(0.04)	(0.04)	(0.04)	(0.04)	(0.03)	(0.03)

Values are means ± (SD)
* $P < 0.05$ vs 60-min value in the same group
C/N and N/C, conventional/new group and new/conventional group, respectively. The fresh gas inlet position was changed at 60 min of the low-flow anesthetic period

tailed *t*-test with a significance level of 0.05, a power level of 0.08 or 0.09, and an anticipated effect size d = difference of means (0.05 or 0.06)/SD (0.03 or 0.04). The required sample size was from six to eight.

Results

Experiment 1

Demographic data were comparable in the four groups in experiment 1 (Table 1). No significant differences in the isoflurane FI/FD ratios were caused by the changed circles in the Dräger NM-GS anesthetic machine (from 0.77 ± 0.08 to 0.77 ± 0.06 in the C/N group; from 0.76 ± 0.03 to 0.78 ± 0.05 in the N/C group; Table 2). However, the isoflurane FI/FD ratios in the new circle of the ACOMA KMA 1300-III anesthetic machine were significantly affected by the changed circles (from 0.61 ± 0.04 to 0.65 ± 0.03 in the C/N group; from 0.65 ± 0.03 to 0.59 ± 0.04 in the N/C group; $P < 0.05$; Table 2).

Experiment 2

There was no significant difference in the demographic data between the two groups in experiment 2 (Table 3). In the 2-h evaluation, the isoflurane FI/FD ratios in the new circle of the ACOMA KMA 1300-III anesthetic machine were significantly higher than these ratios in its conventional circle throughout low-flow anesthesia (1 l·min^{-1} fresh gas flow period), except for the first 40 min ($P < 0.05$; Fig. 2). The mean isoflurane FI/FD ratio in the new and conventional circles were 0.66 ± 0.02 and 0.61 ± 0.04, respectively.

Experiment 3

Demographic data were comparable in the four groups in experiment 3 (Table 3). In the 2-h evaluation, the sevoflurane FI/FD ratios in the new circle of the ACOMA were significantly higher than these ratios in the conventional ACOMA circles from 20 to 80 min after the start of low-flow anesthesia ($P < 0.05$; Fig. 3).

Table 3. Demographic data of patients in experiments 2 and 3

	Machine					
	ACOMA KMA-1300-III				Dräger Fabius	
Anesthesia	ISO	ISO	SEVO	SEVO	SEVO	SEVO
Group	C/C	N/N	C/C	N/N	C/C	N/N
n	7	7	9	9	9	9
Age (years)	63 ± 13	47 ± 17	58 + 15	60 + 13	55 + 15	52 + 11
Sex (M/F)	2/5	3/4	5/4	3/6	2/7	3/6
Height (cm)	154 ± 7	161 ± 7	163 + 11	154 + 9	159 + 9	162 + 11
Weight (kg)	55 ± 11	54 ± 8	64 + 11	56 + 7	59 + 8	60 + 16
BMI (kg/m^2)	23 ± 5	21 ± 4	24 + 6	24 + 3	23 + 3	23 + 4

Values are means ± SD
C/C and N/N, conventional/conventional group and new/new group, respectively; ISO, isoflurane; SEVO, sevoflurane; BMI, means body mass index

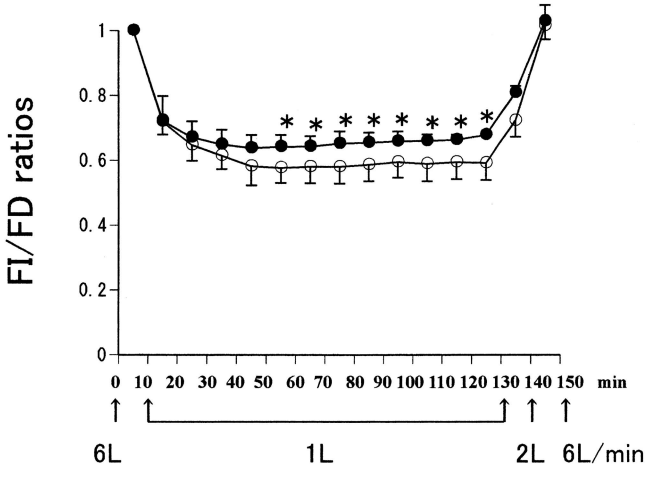

Fig. 2. Inspired fraction/delivered fraction (*FI/FD*) ratios of isoflurane in ACOMA anesthetic machine in experiment 2. *Closed circles* show FI/FD ratios in the new circle, and *open circles* show these ratios in the conventional circle. FI/FD ratios in the new circle were significantly higher than those in the conventional circle. *$P < 0.05$ vs the conventional circle

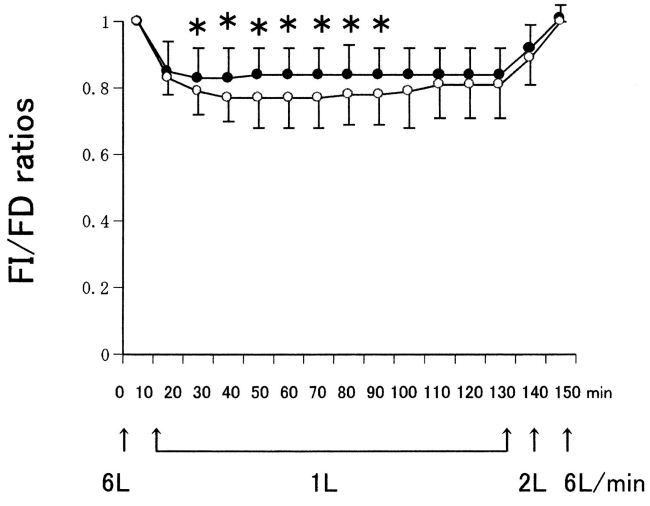

Fig. 3. FI/FD ratios of sevoflurane in ACOMA anesthetic machine in experiment 3. *Closed circles* show FI/FD ratios in the new circle, and *open circles* show these ratios in the conventional circle. FI/FD ratios in the new circle were significantly higher than these in the conventional circle. *$P < 0.05$ vs the conventional circle

In the 2-h evaluation, the sevoflurane FI/FD ratios in the new circle of the Dräger Fabius were significantly higher than those in the conventional Dräger Fabius circles from 80 to 120 min after the start of low-flow anesthesia, except at 100 min ($P < 0.05$; Fig. 4). The mean sevoflurane FI/FD ratios using the ACOMA were 0.84 ± 0.01 (new circle) and 0.79 ± 0.02 (conventional circle). These ratios for the Fabius were 0.82 ± 0.02 (new circle) and 0.80 ± 0.01 (conventional circle).

Discussion

In the present study, we found that positioning the fresh gas inlet between the inspiratory valve and the patient served to improve the FI/FD ratios in low-flow anesthesia. While the changed connection site of the fresh gas inlet was effective for the ACOMA and Fabius machines, this was not the case for the NM-GS. Why was the effect not common to all three anesthetic machines?

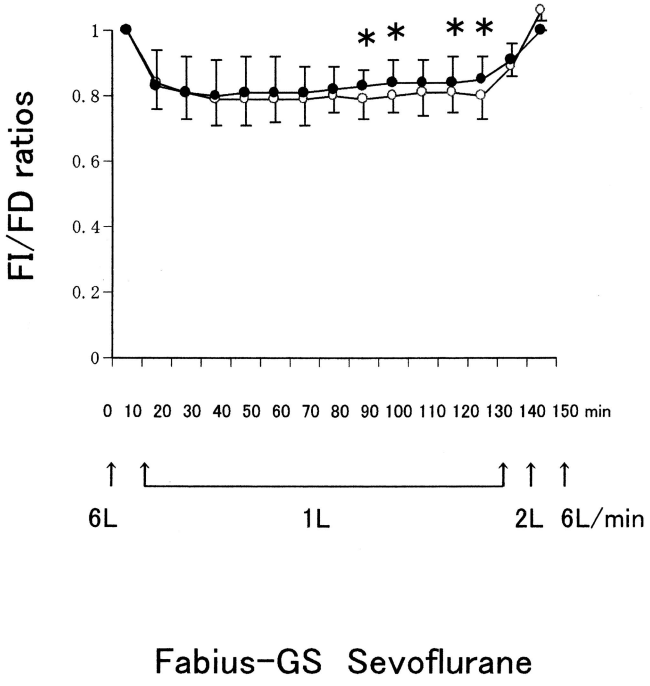

Fig. 4. FI/FD ratios of sevoflurane in the Dräger Fabius-GS anesthetic machine in experiment 3. *Closed circles* show FI/FD ratios in the new circle, and *open circles* show these ratios in the conventional circle. FI/FD ratios in the new circle were significantly higher than those in the conventional circle. $^*P < 0.05$ vs the conventional circle

Figure 1 shows schematic diagrams of the NM-GS, Fabius, and ACOMA anesthetic machines. The most conspicuous difference between the three machines is the connection site of the ventilator. In the ACOMA and Fabius anesthetic machines, a bellows with a unidirectional valve is located between the inspiratory valve and the CO_2 absorber, whereas this bellows is located between the expiratory valve and the CO_2 absorber in the NM-GS anesthetic machine. Because the bellows is dissociated from the fresh gas inlet by a unidirectional valve (decoupling style), in the ACOMA and Fabius anesthetic machines, these machines can maintain a constant tidal volume regardless of the fresh gas flow volume. Therefore, the distance between the fresh gas inlet and inspiratory valve in the conventional circle of the ACOMA and Fabius is functionally longer than that in the NM-GS. We speculate that this difference explains why changing the connection site of the fresh gas inlet was effective only in the ACOMA and Fabius anesthetic machine. Decoupling-style anesthetic machines, such as the ACOMA and Fabius, are not unusual among machines developed for low-flow anesthesia. The decoupling style is used, for example, in the following anesthetic machines: Dogma, Access, Narkomat (Heyer, Bad Ems, Germany), Megamed 700 (Megamed, Cham, Switzerland), SA2 (Dräger), and Sulla909 (Dräger) [4]. In some decoupling-style anesthetic machines, changing the fresh gas inlet connection site might be useful to improve the control of the inhaled gas concentration in low-flow anesthesia.

To our knowledge, two groups have investigated the FI/FD ratios of isoflurane in low-flow anesthesia. Coetzee [5] reported a multicenter study using the Dräger Julian anesthetic machine. In their study, the FI/FD ratio of isoflurane was 0.78 ± 0.15 at a $11 \cdot min^{-1}$ fresh gas flow. Another group used a to-and-fro system, not a circle system, and their FI/FD ratio was 0.52 ± 0.07 at $11 \cdot min^{-1}$ [6]. Two great differences between these two studies [5,6] and ours were the structure of the anesthetic machines and their use of nitrous oxide. It has been reported that nitrous oxide affects the vaporizer output [7]. Although 50% nitrous oxide was used in the above two studies [5,6], we avoided nitrous oxide so as to avoid its adverse influence.

Compared with the mean FI/FD ratio of isoflurane , these ratios of sevoflurane were high, in particular, the FI/FD ratios of sevoflurane in the new circle were more than 0.8 in both the ACOMA and Fabius anesthetic machines. Less soluble anesthetics (e.g., desflurane and sevoflurane) are suitable for low-flow anesthesia, because there is less ongoing uptake and the vaporizer and circuit concentration are closer. Johansson and colleagues [8] reported that the sevoflurane FI/FD ratio of the Servo 900C (Siemens-Elema, Solna, Sweden) was 0.73 ± 0.05 at a fresh gas flow of $11 \cdot min^{-1}$. In regard to desflurane, two investigations have been reported: the FI/FD ratios were 0.80 ± 0.13 and 0.75 ± 0.03 at $11 \cdot min^{-1}$ fresh gas flow [5,9]. Although desflurane is reported to control acute hemodynamic responses to painful surgical stimuli more rapidly than isoflurane in low-flow anesthesia [10], we suggest that sevoflurane is also suitable for low-flow anesthesia, because every sevoflurane FI/FD ratio in our new circle was more than 0.8.

The reason why the ACOMA and Fabius anesthetic machines showed different pattern of changes in the sevoflurane FI/FD ratios is not immediately apparent. In the conventional circle of the ACOMA anesthetic machine, the FI/FD ratios decreased steeply and the difference between the new and conventional circles were remarkable in the early phase of low-flow anesthesia. On the other hand, the sevoflurane FI/FD ratios in the Fabius conventional circle did not change clearly in the early phase of low-flow anesthesia. Significant differences between the Fabius new and conventional circles were observed in the late phase of low-flow anesthesia. We speculate that the different patterns in the sevoflurane FI/FD ratios may be due to the circle or bellows volume. The circle (bellows) volumes of the ACOMA and Fabius machines are about 5.4 l (2.4 l) and 4.3 l (1.4 l), respectively. The large bellows volume of the ACOMA anesthetic machine may explain the steep

decrease of the sevoflurane FI/FD ratio in the early phase. Because the volume of the Fabius anesthetic machine is quite small, sevoflurane uptake may be finished halfway through the low-flow anesthesia (at 120 min). The accumulation of small differences in sevoflurane uptake in the Fabius new circle may lead to earlier saturation and an earlier start in the FI/FD ratio increase than in the conventional circle.

In summary, positioning the fresh gas inlet between the inspiratory valve and the patient improved the FI/FD ratios of isoflurane and sevoflurane at a fresh gas flow of $1 \cdot min^{-1}$ in two decoupling-style anesthetic machines (Dräger Fabius-GS, and ACOMA KMA-1300-III).

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