The Echocardiographic Assessment of Left Ventricular Performance during Sevoflurane and Halothane Anesthesia

Haruyuki KASUDA, Satoshi AKAZAWA and Reiju SHIMIZU

The cardiovascular effects of sevoflurane were studied and compared with those of halothane in 30 healthy patients. The patients were assigned to receive 1 MAC sevoflurane (n=10), 2 MAC sevoflurane (n=10) or 1 MAC halothane (n=10) in N_2O 2 $l \cdot min^{-1}$ and O_2 4 $l \cdot min^{-1}$. The changes in left ventricular diastolic and systolic dimension (Dd and Ds), fractional shortening (FS), mean velocity of circumferential fiber shortening (mVcf), left ventricular diastolic and systolic volume (Vd and Vs), stroke volume (SV), ejection fraction (EF) and cardiac index (CI) were evaluated by echocardiography. Sevoflurane produced significant dose-dependent decreases in FS, mVcf, EF and SV, but no significant changes in Dd and Vd. Therefore, the decrease in SV was due mainly to the increase in left ventricular residual volume (Vs). One MAC halothane produced a more significant decrease in FS, mVcf, EF and SV, when compared to values obtained at 1 MAC sevoflourane ($P < 0.01$). CI was more significantly decreased with 1 MAC halothane than with 1 MAC and 2 MAC sevoflurane ($P < 0.01$). This was brought about by a slight decrease in HR with halothane and a slight increase in HR with sevoflurane, in addition to a smaller decrease in SV with sevoflurane than with halothane. This study suggests that sevoflurane may better preserve cardiac function as a pump in healthy patients, when compared to halothane.
(Key words: echocardiography, halothane, left ventricular function, sevoflurane)

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Sevoflurane is a new, potent, inhaled anesthetic which has a low blood-gas partition coefficient of 0.60[1]. But its clinical safety in cardiovascular system is not established. This study was performed to compare the cardiovascular effects of sevoflurane with those of halothane in healthy patients. In this study, we used noninvasive methods including echocardiography to assess left ventricular performance before and during anesthesia.

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Methods

Thirty patients aged 19 to 55 years scheduled for elective surgical procedures were studied. All the patients had no history of cardiac, pulmonary and other systemic diseases. We explained the study in detail to all the patients, and obtained their consent. This study was approved by the Clinical Research Committee of Jichi Medical School, because there were no expected complications attributable to the procecures.

The patients were randomly assigned to

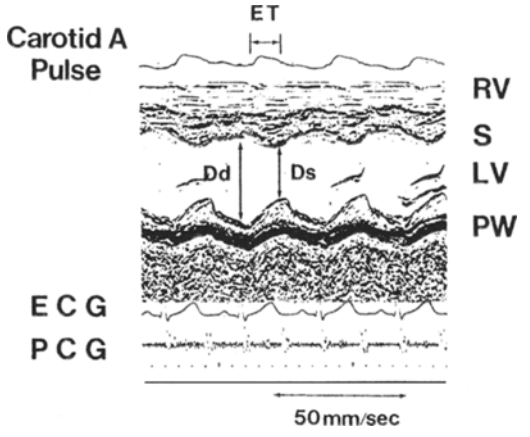

Fig. 1. Typical portion of recordings of echocardiogram of the left ventricle.

Carotid A Pulse: carotid arterial pulse; ECG: electrocardiogram; PCG: phonocardiogram; RV: right ventricle; S: ventricular septum; LV: left ventricular cavity; PW: posterior left ventricular wall; ET: left ventricular ejection time; Dd: left ventricular diastolic dimension; Ds: left ventricular systolic dimension.

receive 1 MAC sevoflurane (Group S-1, n=10), 2 MAC sevoflurane (Group S-2, n=10) or 1 MAC halothane (Group H-1, n=10). The patients in all groups were premedicated with atropine, 0.5 mg, and hydroxizine, 50 mg, intra-muscularly forty minutes before the induction of anesthesia. In the operating room, a Dinamap® blood pressure cuff, electrocardiographic leads, phonocardiographic probe and carotid arteriographic probe were applied to the patients. Before induction of anesthesia, heart rate (HR), mean blood pressure (mAP), electrocardiography, phonocardiography, carotid arteriography and echocardiography were measured in the patients breathing room air.

Anesthesia was induced with 2–5% sevoflurane or 1–2% halothane in N_2O 4 $l \cdot min^{-1}$ and O_2 2 $l \cdot min^{-1}$ via a mask. Succinylcholine, 1 $mg \cdot kg^{-1}$, was administered intravenously to facilitate orotracheal intubation. The patients were ventilated to control end-tidal carbon dioxide concentration between 35 and 40 mmHg. End-tidal anesthetic concentrations were respectively maintained at 1.7% (1 MAC) sevoflurane[2], 3.4% (2 MAC) sevoflurane or 0.75% (1 MAC) halothane[3] in N_2O 4 $l \cdot min^{-1}$ and O_2 2 $l \cdot min^{-1}$. HR, mAP, electrocardiogramAP, electrocardiography, phonocardiography, carotid arteriography and echocardiography were measured after 15 min stabilization of end-tidal anesthetic concentration. End-tidal anesthetic gas and carbon dioxide concentrations were measured by Normac Multigas Monitor® (Datex Co. Ltd.) which was calibrated for a linear reponse for each gas concentration using a gaschromatography. Surgical stimulation was avoided throughout the course of the study.

The echocardiography were performed by means of Aloka SSD-730 ultrasonoscope. A 3.5 MHz transducer of 10 mm in diameter was applied to the patients in the supine or

Table 1. Demographics

	Group S-1 (n=10)	Group S-2 (n=10)	Group H-1 (n=10)
Anesthetics	sevoflurane 1 MAC in N_2O 4 $l \cdot min^{-1}$ & O_2 2 $l \cdot min^{-1}$	sevoflurane 2 MAC in N_2O 4$l \cdot min^{-1}$ & O_2 2$l \cdot min^{-1}$	halothane 1 MAC in N_2O 4$l \cdot min^{-1}$ & O_2 2$l \cdot min^{-1}$
Age (Yr)	32.1 ± 13.0 (19–58)	28.6 ± 11.6 (19–55)	32.9 ± 12.0 (18–46)
Height (cm)	156.0 ± 5.6 (140–165)	159.8 ± 6.6 (148–169)	160.1 ± 6.0 (150–174)
Weight (kg)	56.1 ± 10.4 (41–80)	59.3 ± 7.6 (40–75)	56.6 ± 10.6 (42–85)
Male:Female	4:6	6:4	4:6

Values are given as mean ± SD and ranges in parenthesis.

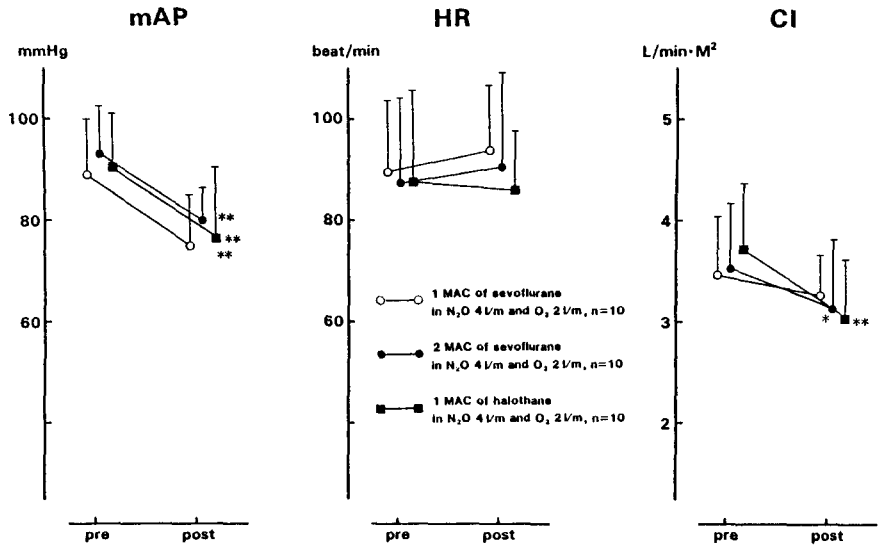

Fig. 2. Changes in mean arterial pressure (mAP), heart rate (HR) and cardiac index (CI) at 1 MAC of sevoflurane (open circles), 2 MAC of sevoflurane (closed circles) or 1 MAC of halothane (closed squares) in N_2O 4 $l \cdot min^{-1}$ and O_2 2 $l \cdot min^{-1}$. All values are mean ± SD.
*: $P < 0.05$ vs control **: $P < 0.01$ vs control

the left lateral decubitus position. To examine the left ventricle (LV), the echocardiographic transducer was positioned perpendicular to the chest at the left parasternal border in the third or fourth intercostal space; the two-dimensional sector scan was aligned to the long axis of the left ventricle; and the M-mode beam was directed inferiorly from the position where the mitral valve was detected. At the level of the chordae tendineae, the right ventricular cavity, the interventricular septum (IVS), and the posterior wall of LV were transected by the echocardiographic beam and M-mode echocardiograms were recorded on a strip chart recorder at a paper speed of 50 mm·sec.

The LV echocardiographic dimensions were represented by the distances from the endocardial echo of the posterior LV wall to the endocardial echo of the LV side of the IVS. LV diastolic dimension (Dd) was measured at the peak of R wave of the electrocardiogram, and LV systolic dimension (Ds) was measured at the second sound of the phonocardiogram (fig. 1). The mean values of them in three or four successive cardiac cycles were used for the following calculations.

$V=7D^3/(2.4+D)$
(the Teichholz formula[4], V: LV volume, D: LV dimension)

$FS=(Dd - Ds)/Dd \times 100$
(FS: fractional shortening)

$mVcf=(Dd - Ds)/(Dd \times LVET)$
(mVcf: mean velocity of circumferential fiber shortening, LVET: LV ejection time)

$SV=Vd-Vs$
(SV: stroke volume, Vd: diastolic V, VS: systolic V)

$EF=(Vd-Vs)/Vd \times 100$
(EF: ejection fraction)

$CI=(SV \times HR)/BSA$
(CI: cardiac index, BSA: body surface area)

$SVRI=mAP/CI$
(SVRI: systemic vascular resitance index)

LVET was determined from carotid arterial pulse recording which represents the time from the beginning of the upstroke of arterial pulse to the dicrotic notch (fig. 1).

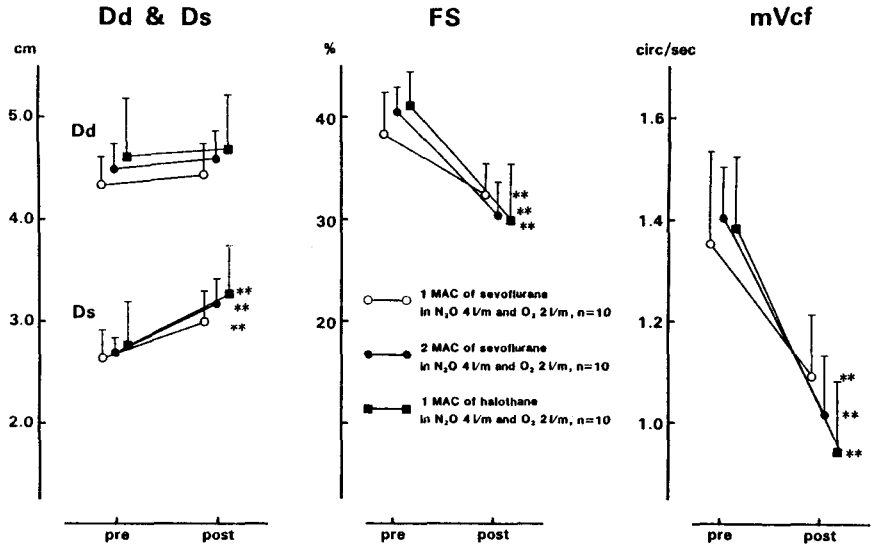

Fig. 3. Changes in left ventricular diastolic and systolic dimension (Dd and Ds), fractional shortening (FS) and mean velocity of circumferential fiber shortening (mVcf) at 1 MAC of sevoflurane (open circles), 2 MAC of sevoflurane (closed circles) or 1 MAC of halothane (closed squares) in N_2O 4 $l \cdot min^{-1}$ and O_2 2 $l \cdot min^{-1}$. All values are mean ± SD.
*: $P < 0.05$ vs control **: $P < 0.01$ vs control

Results are expressed as mean ± SD. Statistical comparison with preanesthetic values was assessed by paired Student's t-test. Comparisons between groups were by the X^2 test, and unpaired Student's t-test or Welch's t-test when appropriate[5]. A P value of 0.05 was accepted as statistically significant.

Results

The patients in each group were comparable with respect to age, sex, weight and height (table 1). Pre-and post anesthetic data for hemodynamic and echocardiographic variables are presented in table 2. There were no significant differences between the groups with regard to the preanesthetic values of HR, mAP and echocardiographic parameters.

After inhalation of anesthetics, mAP significantly decreased in every group ($P < 0.01$) (fig. 2). HR showed a tendency to increase, but not significantly, in Group S-1 and S-2, whereas it showed a tendency to decrease, but not significantly, in Group H-1. With regard to the changes in HR, a significant difference was found between Group H-1 and the other groups ($P < 0.05$).

Dd did not change in every group (fig. 3). Ds increased in every group ($P < 0.01$), and the increase in Ds was greater in Group H-1 than in Group S-1 ($P < 0.05$). FS decreased in every group ($P < 0.01$), and the decrease in FS was greater in Group S-2 and H-1 than in Group S-1 ($P < 0.05$ and 0.01, respectively). mVcf decreased in every group ($P < 0.01$), and the decrease in mVcf was greater in Group S-2 and H-1 than in Group S-1 ($P < 0.05$ and 0.01, respectively).

Vd did not change in every group (fig. 4). Vs increased in every group ($P < 0.01$), and the increase in Vs was greater in Group S-2 and H-1 than in Group S-1 ($P < 0.05$). SV decreased in every group ($P < 0.01$), and the decrease in SV was greater in Group S-2 and H-1 than in Group S-1 ($P < 0.05$ and 0.01, respectively). EF decreased in every group ($P < 0.01$), and the decrease in EF was greater in Group S-2 and H-1 than in Group S-1 ($P < 0.05$ and 0.01, respectively).

Table 2. Changes in cardiovascular variables

		before anesthesia	during anesthesia	difference
Mean arterial pressure (mAP, mmHg)	Group S-1	89.8 ± 10.3	76.4 ± 10.0**	−13.4 ± 9.4
	Group S-2	91.5 ± 9.5	78.4 ± 7.2**	−13.1 ± 7.2
	Group H-1	88.2 ± 9.6	75.7 ± 12.7**	−12.5 ± 7.2
Heart rate (HR, beats·min^{-1})	Group S-1	87.7 ± 12.7	93.6 ± 12.6	5.9 ± 9.1
	Group S-2	85.2 ± 14.7	90.8 ± 17.1	5.6 ± 7.6
	Group H-1	87.5 ± 15.3	84.4 ± 10.1	−3.1 ± 7.8†‡
Left ventricular diastolic dimension (Dd, cm)	Group S-1	4.36 ± 0.26	4.44 ± 0.33	0.10 ± 0.16
	Group S-2	4.51 ± 0.22	4.58 ± 0.27	0.07 ± 0.26
	Group H-1	4.62 ± 0.46	4.64 ± 0.46	0.02 ± 0.08
Left ventricular systolic dimension (Ds, cm)	Group S-1	2.66 ± 0.26	3.01 ± 0.30**	0.31 ± 0.21
	Group S-2	2.68 ± 0.16	3.20 ± 0.23**	0.52 ± 0.28
	Group H-1	2.80 ± 0.39	3.32 ± 0.42**	0.52 ± 0.12†
Fractional shortening (FS, %)	Group S-1	39.0 ± 3.6	32.4 ± 3.2**	−6.7 ± 1.4
	Group S-2	40.5 ± 2.4	30.5 ± 3.3**	−9.9 ± 3.5†
	Group H-1	39.4 ± 4.1	28.5 ± 5.1**	−10.9 ± 3.4††
Mean velocity of circumferential fiber shortening (mVcf, circ·sec^{-1})	Group S-1	1.35 ± 0.18	1.09 ± 0.12**	−0.27 ± 0.07
	Group S-2	1.40 ± 0.10	1.01 ± 0.12**	−0.39 ± 0.15†
	Group H-1	1.34 ± 0.15	0.90 ± 0.14**	−0.45 ± 0.14††
Left ventricular diastolic volume (Vd, ml)	Group S-1	86.3 ± 12.2	90.3 ± 15.2	4.0 ± 6.9
	Group S-2	93.0 ± 11.5	96.6 ± 13.4	3.6 ± 12.1
	Group H-1	98.8 ± 23.1	100.2 ± 23.0	1.4 ± 3.3
Left ventricular systolic volume (Vs, ml)	Group S-1	26.2 ± 6.2	35.9 ± 8.6**	9.7 ± 3.8
	Group S-2	26.7 ± 3.7	41.2 ± 7.6**	14.5 ± 8.5†
	Group H-1	30.5 ± 10.2	45.6 ± 13.6**	15.1 ± 4.9†
Stroke volume (SV, ml)	Group S-1	60.1 ± 7.8	54.4 ± 8.2**	−5.2 ± 5.0
	Group S-2	66.3 ± 9.4	55.4 ± 9.8**	−10.9 ± 8.6†
	Group H-1	68.3 ± 14.6	54.6 ± 13.5**	−13.7 ± 6.2††
Ejection fraction (EF, %)	Group S-1	69.9 ± 4.2	60.5 ± 4.4**	−8.4 ± 3.3
	Group S-2	71.2 ± 2.8	57.2 ± 5.5**	−14.0 ± 5.9†
	Group H-1	69.8 ± 4.9	54.6 ± 6.3**	−15.2 ± 5.1††
Cardiac index (CI, l/min·m^2)	Group S-1	3.49 ± 0.66	3.28 ± 0.40	−0.21 ± 0.48
	Group S-2	3.48 ± 0.59	3.10 ± 0.63*	−0.38 ± 0.50†
	Group H-1	3.69 ± 0.56	2.88 ± 0.57**	−0.82 ± 0.26†††‡‡
Systemic vascular resistance index (SVRI, mmHg·min·L^{-1}·m^2)	Group S-1	26.2 ± 5.1	23.1 ± 4.7	3.1 ± 2.4
	Group S-2	27.4 ± 5.6	26.6 ± 5.6	0.8 ± 2.9
	Group H-1	24.4 ± 4.9	27.0 ± 5.8	−2.6 ± 3.8

All values are mean ± SD
* & **: $P < 0.05$ & $P < 0.01$ vs control
† & ††: $P < 0.05$ & $P < 0.01$ vs Group S-1
‡ & ‡‡: $P < 0.05$ & $P < 0.01$ vs Group S-2
difference indicates the one between before and during anesthesia

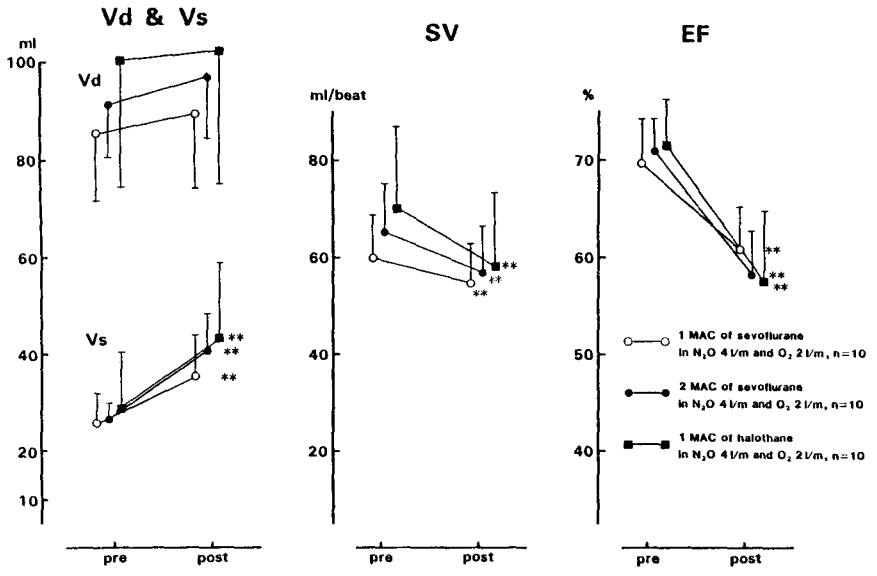

Fig. 4. Changes in left ventricular diastolic and systolic volume (Vd and Vs), stroke volume (SV) and ejection fraction (EF) at 1 MAC of sevoflurane (open circles), 2 MAC of sevoflurane (closed circles) or 1 MAC of halothane (closed squares) in N_2O 4 $l \cdot min^{-1}$ and O_2 2 $l \cdot min^{-1}$. All values are mean ± SD.
*: $P < 0.05$ vs control **: $P < 0.01$ vs control

CI decreased in Group S-2 and H-1 ($P < 0.05$ and 0.01, respectively), but did not change in Group S-1 (fig. 2). The decrease in CI was greater in Group H-1 than in Group S-1 and S-2 ($P < 0.01$), and the decrease in CI was greater in Group S-2 than in Group S-1 ($P < 0.05$). There was no significant changes in SVRI in every group.

Discussion

Serial echocardiographic measurements of myocardial function must be carefully interpreted because HR, preload, afterload, and contractility may independently or synergically influence the dimensions of the left ventricle and other hemodynamic parameters. HR did not show the significant difference between before and during anesthesia in all groups; therefore, HR was not a major factor contributing to the change in left ventricular function. The effect of sevoflurane and halothane on preload remains obscure. In clinical studies using echocardiography to assess preload status, Rathod et al.[6] found a significant decrease in Dd, whereas Gerson et al.[7] noted a significant increase in Dd under halothane anesthesia. In our study (sevoflurane and halothane) and previous reports by Barash et al.[8] (halothane) and by Wolf et al. (halothane and isoflurane)[9], there were no significant changes in Dd and Vd, suggesting that preload remained relatively constant.

As we used only noninvasive methods in this study, neither right atrial pressure nor central venous pressure was measured. But we thought changes in central venous pressure were relatively small or negligible in this study, because we could not catch any clinical sign suggesting changes in venous pressure.; therefore, SVRI was calculated as the quotient of mAP and CI. In human studies, halothane does not characteristically change total systemic vascular resistance[10,11], whereas both isoflurane and enflurane cause vasodilation with a fall in systemic vascular resistance[12,13]. In this study, SVRI did not change significantly, suggesting afterload remains relatively constant during both sevoflurane and halothane anesthesia. In all of three groups in our

study, HR, preload and afterload were relatively constant; therefore, the changes observed by the echocardiographic measurements mainly reflect alterations in contractility.

Sevoflurane produced significant dose-dependent decreases in FS, mVcf, EF and SV. This indicates that sevoflurane depressed left ventricular function with increasing depth of anesthesia, as with other inhalation anesthetics[10–13]. Decreases in FS, mVcf, EF and SV were due mainly to increases in Ds or Vs, because Dd and Vd were not significantly altered by sevoflurane. The increase in Vs was indicative of diminished emptying of the left ventricle i.e., the increase in left ventricular residual volume.

Halothane produced a more significant decrease in FS, mVcf, EF and SV than sevoflurane. This indicates that sevoflurane did not depress left ventricular function as strongly as halothane in healthy patients and coincided with the result of animal study in which LV dp/dt max was measured by Millar Micro-Tip catheter pressure transducer[14].

When mAP was significantly decreased by inhalation anesthetics, HR showed a tendency to increase in Group S-1 and S-2, but to decrease in Group H-1. Although HR showed a dose-dependent decrease[15] or unsignificant changes[14,16] in animals, HR showed a tendency to increase in a multicenter clinical trial of sevoflurane in 244 healthy patients[17]. In ths study, the changes in HR was reflected in the changes in CI. CI was not significantly decreased in Group S-1 (1 MAC sevoflurane). The decrease in CI was greater in Group H-1 (1 MAC halothane) than in Group S-2 (2 MAC sevoflurane). This smaller decrease in CI with sevoflurane was due to a combination of a slight decrease in SV and a slight increase in HR. Baroreceptor reflexes are depressed by halothane[18], halothane with nitrous oxide[19], and enflurane with or without nitrous oxide[20]. The depressive effect of isoflurane on the baroreceptor reflex was not likely to be as strong as that of halothane or enflurane[21]. At present, it is not clarified whether sevoflurane depresses baroreflex control of HR or not. Judging from the results of this study, it seems that this reflex was preserved better during sevoflurane anesthesia in healthy patients, when compared to during halothane anesthesia.

In conclusion, cardiac function, especially pump function (CI), may be preserved better in healthy patients under sevoflurane anesthesia, when compared to halothane. A small reduction in CI may be due probably to a combination of a slight decrease in SV and a slight increase in HR.

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