Different effects of sevoflurane, desflurane, and isoflurane on early and late left ventricular diastolic function in young healthy adults†

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Background. Knowledge on the effects of volatile anaesthetics on left ventricular (LV) diastolic function in humans in vivo is limited. We tested the hypothesis that sevoflurane, desflurane, and isoflurane do not impair LV diastolic function in young healthy humans.

Methods. Sixty otherwise healthy subjects (aged 18–48 yr) undergoing minor procedures under general anaesthesia were studied. After randomization for the anaesthetic, transthoracic echocardiographic examinations were performed at baseline and under anaesthesia with 1 minimum alveolar concentration (MAC) of the volatile anaesthetics during spontaneous breathing and intermittent positive pressure ventilation (IPPV). Peak early (E) and late (A) diastolic velocities of the mitral annulus were studied as the main echocardiographic indicators of diastolic function.

Results. During anaesthesia with 1 MAC under spontaneous breathing, E increased with desflurane (P<0.001), was not significantly different with isoflurane (P=0.030), and decreased with sevoflurane (P=0.006). During IPPV, E was similar to baseline with desflurane (P=0.550), insignificantly decreased with isoflurane (P=0.029), and decreased with the sevoflurane group (P<0.001). In contrast, A was similarly reduced in all groups during spontaneous breathing without further changes during IPPV. Haemodynamic changes were comparable in all study groups.

Conclusions. The findings of this in vivo study indicate that desflurane and isoflurane, and most likely sevoflurane, do not have a relevant direct negative impact on early diastolic relaxation in young healthy humans. In contrast, all three volatile anaesthetics appear to impair late diastolic LV filling during atrial contraction.

Trial Registration #: NCT0024451.

Keywords: anaesthetics volatile, desflurane; anaesthetics volatile, isoflurane; anaesthetics volatile, sevoflurane; heart, myocardial function; monitoring, echocardiography

Accepted for publication: February 24, 2010

Volatile anaesthetics induce complex cardiovascular effects and alter calcium homeostasis. However, there are conflicting results regarding their effects on diastolic function in animals, healthy humans, and patients. Whereas some animal studies found direct impairment of diastolic myocardial relaxation and ventricular filling by volatile anaesthetics, others found indirect negative effects on diastolic function caused by depression of systolic left ventricular (LV) function in canine models. Two studies in patients with coronary artery disease (CAD) found impairment of diastolic relaxation by isoflurane, desflurane, sevoflurane, and halothane, whereas another study in patients with concentric LV hypertrophy found no additional impairment of diastolic function with isoflurane. Our own group found an impairment of systolic but not diastolic function with sevoflurane in young healthy subjects and in patients with pre-existing diastolic dysfunction, and with halothane in young healthy subjects.

†Parts of the data were presented at the Annual Meeting of the European Association of Cardiothoracic Anaesthesiologists EACTA 2009 in Athens, Greece.
Taken together, the influence of currently used volatile anaesthetics on diastolic function is unclear, and volatile anaesthetics might affect cardiac function differently. Pre-existing cardiac diseases and differences in cardiac loading conditions might have led to these conflicting results in the assessment of the effects of volatile anaesthetics on diastolic function. Therefore, the aim of this study was to evaluate for the first time the effect of the currently used volatile anaesthetics, sevoflurane, desflurane, and isoflurane on diastolic function in healthy young subjects in vivo under standardized and controlled loading and haemodynamic conditions. On the basis of our previous findings, we hypothesized that none of these volatile anaesthetics impairs LV diastolic function in healthy young subjects.

Methods

Patients

After receiving approval by the local ethics committee (Ethikkommission beider Basel, Basel, Switzerland) and obtaining written informed consent, 61 patients undergoing minor surgical procedures under general anaesthesia were enrolled (Fig. 1). Exclusion criteria were any history or signs of cardiac, pulmonary, or systemic disease, any medication with cardiovascular effects or side-effects, age <18 or >50 yr, and BMI >30 kg m⁻². A computer-generated random list was used to assign patients to sevoflurane, desflurane, or isoflurane anaesthesia after performing the baseline transthoracic echocardiography (TTE). No premedication was given. After arrival in the preoperative area, i.v. access was established, and Ringer’s lactate was administered to replace the fluid deficit caused by overnight fasting. The deficit per hour of fasting was calculated as follows: 4 ml kg⁻¹ h⁻¹ for the first 10 kg of body weight, 2 ml kg⁻¹ h⁻¹ for the second 10 kg, and 1 ml kg⁻¹ h⁻¹ for every additional kilogram. Fifty per cent of the deficit was replaced before the start of the study and a total of 66% until the end of the study. To minimize nausea and vomiting potentially caused by induction of anaesthesia, tropisetrone 4 mg (Navoban®; Novartis Pharma, Basel, Switzerland) was given to each patient as soon as i.v. access was established. Two-lead electrocardiography and pulse oximetry were monitored continuously, and arterial pressure was measured non-invasively every 3 min (PCMS Workstation 90308-15-03, SpaceLab Inc., Redmond, WA, USA). Simultaneously, biespectral index (BIS™; Aspect 1000™, Aspect Medical Systems Inc., Natick, MA, USA; Software Version 1.01) was monitored continuously. Upon induction of anaesthesia, end-tidal concentrations of carbon dioxide (P₄CO₂) and volatile anaesthetic were measured continuously at the tip of the laryngeal mask (Capnomac Ultima, Datex Ohmeda, Helsinki, Finland). Body temperature was measured continuously and maintained above 36°C. Hypotension, defined as a decrease of >30% from baseline value in mean arterial pressure, was treated with i.v. boluses of phenylephrine 25–50 μg. Hypertension, defined as an increase of >30% from baseline value in mean arterial pressure, was treated with i.v. boluses of nitroglycerine 25–50 μg. To minimize influence on echocardiographic measurements, the study was continued no earlier than 5 min after administration of any vasoactive medication. Tachycardia or bradycardia was not treated, but the study was continued only when heart rate recovered to values between 50 and 90 beats min⁻¹.

The baseline TTE was performed in the awake and unpremedicated patient in a partial left lateral position. The same position was used during all further measurements. After completion of the baseline TTE, anaesthesia was induced by i.v. infusion of remifentanil (Ultiva®, GlaxoSmithKline, London, UK) delivered by a target-controlled infusion system (Orchestra® Base Primera, Fresenius Vial, Brezins, France)
beginning at a calculated end-organ concentration of 1.5 ng ml$^{-1}$ and increased to 2.0 ng ml$^{-1}$. One hundred percent oxygen was delivered by a facemask. Afterwards, induction was completed by inhalation of sevoflurane (Sevorane®, Abbott International Ltd, Abbott Park, IL, USA), desflurane (Suprane®), Baxter, Deerfield, IL, USA), or isoflurane (Forane®, Abbott International Ltd). No other narcotics, opioids, or neuromuscular blocking agents were used. After placement of a laryngeal mask, the inspiratory oxygen concentration was adjusted to 40%, the remifentanil infusion was stopped, and the administration of volatile anaesthetics was reduced to an end-tidal concentration corresponding to 1 minimum alveolar concentration (MAC). The MAC value was age-adjusted according to the formula published by Eger. As soon as remifentanil end-organ concentration in the patient reached <0.1 ng ml$^{-1}$ (as calculated by the target-controlled infusion system), and anaesthetic and haemodynamic steady-state conditions were reached, a second TTE was performed under spontaneous breathing (step I). After completion of data acquisition, intermittent positive pressure ventilation (IPPV) via the laryngeal mask was started to achieve normoventilation ($P_{\text{ETCO}_2}$ 4.5–5.0 kPa). Tidal volumes were adjusted to 7–8 ml kg$^{-1}$. The concentration of the volatile anaesthetic was kept at 1.0 MAC. During haemodynamic steady-state conditions, a third TTE (step II) was performed, completing the study. Subsequently, each patient underwent surgery and anaesthesia, which was not influenced by the study protocol.

Echocardiography

All echocardiograms were obtained with a Sonos$^\text{TM}$ 5500 ultrasonographic system and a 1.8–2.1/3.6–4.1 MHz S4 probe (Philips Medical Systems, Best, the Netherlands) according to current guidelines. All echocardiographic data were digitally stored for subsequent off-line analysis. In the same patient, one examiner performed all TTE examinations. Standard LV short-axis and two- and four-chamber views were obtained by the parasternal and apical views for TTE. For recordings of pulsed-wave tissue Doppler imaging, the sample volume was placed at the septal (as indicated on left-hand side) and lateral sides of the mitral annulus. The tissue Doppler signal reflects the movements of the mitral annulus and shows two diastolic ($E'$ and $A'$) and a systolic peak ($S'$). $E'$ reflects early filling phase, whereas $A'$ is related to atrial contraction. LA, left atrium; LV, left ventricle.

![Figure 2](image.png)

**Fig 2** Recordings of pulsed-wave tissue Doppler imaging. The sample volume was placed at the septal (as indicated on left-hand side) and lateral sides of the mitral annulus. The tissue Doppler signal reflects the movements of the mitral annulus and shows two diastolic ($E'$ and $A'$) and a systolic peak ($S'$). $E'$ reflects early filling phase, whereas $A'$ is related to atrial contraction. LA, left atrium; LV, left ventricle.

Statistical analysis

The sample size calculation was based on our previous study, estimating that a size of 20 patients per group...
Continuous variables are presented as means (SD) and dichotomous variables as values (%). The Kolmogorov–Smirnov statistics showed a normal distribution for all continuous echocardiographic and patient characteristic data in each group. Baseline parameters were compared by χ² test or one-way analysis of variance (ANOVA) where appropriate. A general linear model for repeated measurements was used to test the null hypothesis of lack of differences between the study groups and within the study groups. Only if the model gave global evidence for rejection of the null hypothesis at a P-value of <0.05, the data were further analysed by ANOVA for repeated measurements followed by Bonferroni’s post hoc test for differences of the data during steps I and II compared with the baseline (within-group differences; a P-value of <0.025 was considered significant). Similarly, data were further analysed for differences between the study groups by one-way ANOVA and Bonferroni’s post hoc test (inter-group differences; a P-value of <0.025 was considered significant). All statistical analyses were performed using SPSS 16.0 (SPSS Inc., Chicago, IL, USA).

Results

One subject had an E' <8.5 cm s⁻¹ and an E/A ratio <1 in the baseline TTE, suggesting LV diastolic dysfunction and was excluded from the further study, leaving 60 subjects (20 in each group). All groups had similar patient characteristics except that the desflurane group was slightly younger (Table 1).

The study was performed in all subjects without complications occurring during or after the study. One subject in the desflurane group and one subject in the sevoflurane group did not reach stable haemodynamic conditions during IPPV because 1 MAC of the volatile anaesthetic provided insufficient depth of anaesthesia for performing mechanical ventilation. Accordingly, step II could not be performed in these two subjects.

Baseline haemodynamic and echocardiographic parameters were similar in all groups (Table 2).

Table 1 Subject characteristics. Values are expressed as numbers (%), mean (range) or mean (SD). P-values were calculated by χ² test or one-way ANOVA.

<table>
<thead>
<tr>
<th></th>
<th>Sevoflurane (n=20)</th>
<th>Desflurane (n=20)</th>
<th>Isoflurane (n=20)</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Female gender</td>
<td>7 (35)</td>
<td>8 (40)</td>
<td>5 (25)</td>
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<tr>
<td>Age (yr)</td>
<td>32 (18–48)</td>
<td>27 (19–46)</td>
<td>34 (20–48)</td>
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<tr>
<td>Weight (kg)</td>
<td>73 (15)</td>
<td>69 (10)</td>
<td>72 (11)</td>
<td>0.424</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>176 (11)</td>
<td>174 (9)</td>
<td>174 (9)</td>
<td>0.781</td>
</tr>
<tr>
<td>Haemoglobin (g litre⁻¹)</td>
<td>148 (14)</td>
<td>146 (12)</td>
<td>146 (20)</td>
<td>0.926</td>
</tr>
<tr>
<td>Creatinine (μmol litre⁻¹)</td>
<td>69 (12)</td>
<td>67 (12)</td>
<td>70 (18)</td>
<td>0.867</td>
</tr>
</tbody>
</table>

Effects of volatile anaesthetics during spontaneous breathing (step I) and IPPV (step II)

Haemodynamics, BIS, and P_{CO₂} changed similarly in all groups (Table 2). Phenylephrine but no other vasoactive medication was administered during the study to three subjects in the sevoflurane group (100–300 μg), to two subjects in the desflurane group (25–500 μg), and to no subjects in the isoflurane group (P=0.189; χ² test).

During step I, E' significantly increased compared with baseline in the desflurane group (P<0.001), was not significantly different in the isoflurane group (P=0.030), and decreased in the sevoflurane group (P=0.006). During step II, E' was similar to baseline in the desflurane group (P=0.550), insignificantly decreased in the isoflurane group (P=0.029), and decreased in the sevoflurane group (P<0.001). During both steps I and II, E' was similar in the isoflurane and sevoflurane groups (P=0.300 and 0.131, respectively), but significantly higher in the desflurane group (all P<0.003) (Fig. 3A). The E' values of all subjects and groups were within normal range at baseline and during step I, and only one subject of the sevoflurane group had an E' value of <8.5 cm s⁻¹, indicating diastolic dysfunction (21–23) during step II. The changes in E and IVRT went in parallel to E' (Table 2).

Late diastolic velocity A' was similarly decreased in all groups during step I, compared with baseline (all P>0.015). This reduction in late diastolic velocity was further pronounced during step II (Fig. 3B) with an additional small difference between the isoflurane and desflurane groups (P=0.006). The changes in A developed in parallel to A'.

The effects of sevoflurane, desflurane, and isoflurane on EDA and E/E' were similar, and the E/E' ratio was below 10 in all subjects. Accordingly, there was no evidence for differences in loading conditions or for elevated filling pressures. Further, the effects of volatile anaesthetics on E/A, FAC, and S' did not differ (Table 2).

Intra- and inter-observer variabilities for the different echocardiographic parameters are given in Table 3.

Discussion

The present study used diastolic tissue Doppler echocardiographic parameters to investigate the effects of 1 MAC of sevoflurane, desflurane, and isoflurane on LV diastolic function in young healthy subjects with normal diastolic and systolic LV function. E' reflects mitral annular motion during the rapid early filling phase. This parameter is related to the rate of myocardial relaxation and correlates with τ,22 the time constant of the decrease in LV isovolumetric pressure; A' is the annular velocity occurring during the late filling phase, which is related to active atrial contraction and, therefore, can be used as a marker for global systolic atrial function.22,24 A' correlates well with atrial ejection fraction, ejection force, and kinetic energy.24–26
The exception of one patient, who remained with normal is, early diastolic function was significantly impaired but with slightly decreased in the sevoflurane group (Fig. 3A), which was similar in other groups. Under isoflurane anaesthesia with 1 MAC of each volatile anaesthetic during spontaneous breathing, with 1 MAC of each volatile anaesthetic, diastolic function was slightly higher than in the control group, but was not different compared with the sevoflurane and desflurane groups. In the desflurane group, early diastolic function was slightly improved in the desflurane group compared with the control group. Early diastolic function was slightly improved in the desflurane group compared with the control group.

We found that under standardised loading conditions, the

<table>
<thead>
<tr>
<th>Group</th>
<th>Step I</th>
<th>Step II</th>
<th>Step III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoflurane</td>
<td>65 (8)</td>
<td>63 (13)</td>
<td>59 (8)</td>
</tr>
<tr>
<td>Sevoflurane</td>
<td>66 (8)</td>
<td>69 (11)</td>
<td>67 (10)*</td>
</tr>
<tr>
<td>Desflurane</td>
<td>72 (9)*</td>
<td>75 (13)*</td>
<td>73 (13)*</td>
</tr>
</tbody>
</table>


t-test for differences vs 0

P<0.001 0.001 0.001 0.001

Table 2: Haemodynamics and echocardiographic parameters at baseline and during step I and II. Values are expressed as median (IQR). P<0.05 between groups. ΔP<0.05 between groups vs baseline. ΔE vs baseline. ΔE vs sevoflurane vs desflurane. ΔE vs step I and II compared with the baseline. ΔE, end-tidal carbon dioxide partial pressure; N/A, not available. For abbreviations of echocardiographic parameters, see text.

### Table 3: Intraobserver variability of echocardiographic parameters (95% CI). For abbreviations of echocardiographic parameters, see text.

| Parameter | Mean (IQR) | N/A | P<0.001 0.001 0.001 0.001 0.001

| Mean (IQR) | N/A | P<0.001 0.001 0.001 0.001 0.001

| Parameter | Mean (IQR) | N/A | P<0.001 0.001 0.001 0.001 0.001

| Parameter | Mean (IQR) | N/A | P<0.001 0.001 0.001 0.001 0.001

**Fig 3** Mean absolute changes and 95% CI for peak early (AE) and late diastolic velocity (AVA) of the mitral annulus at baseline and during step I and II.

* indicates significant difference between sevoflurane and desflurane on Fig 3A and 3B.

**Table 4:** Changes in heart rate (HR), BIS, NCCO, cardiac output (CO), and central venous pressure (CVP) during step I and II.

| Parameter | Mean (IQR) | N/A | P<0.001 0.001 0.001 0.001 0.001

| Parameter | Mean (IQR) | N/A | P<0.001 0.001 0.001 0.001 0.001

| Parameter | Mean (IQR) | N/A | P<0.001 0.001 0.001 0.001 0.001

| Parameter | Mean (IQR) | N/A | P<0.001 0.001 0.001 0.001 0.001

**Table 5:** Changes in intraobserver variability of echocardiographic parameters (95% CI). For abbreviations of echocardiographic parameters, see text.

| Parameter | Mean (IQR) | N/A | P<0.001 0.001 0.001 0.001 0.001

| Parameter | Mean (IQR) | N/A | P<0.001 0.001 0.001 0.001 0.001

| Parameter | Mean (IQR) | N/A | P<0.001 0.001 0.001 0.001 0.001

| Parameter | Mean (IQR) | N/A | P<0.001 0.001 0.001 0.001 0.001

**Fig 4** Mean absolute changes and 95% CI for peak early (AE) and late diastolic velocity (AVA) of the mitral annulus at baseline and during step I and II.

* indicates significant difference between sevoflurane and desflurane on Fig 4A and 4B.
limits. In contrast to the variable effects of the volatile anaesthetics on early LV relaxation, we found evidence that each of the volatile anaesthetics impaired global diastolic function as apparent by decreases in $A'$ during spontaneous ventilation and IPPV. Impairment of systolic atrial function potentially impairs late diastolic LV function (Fig. 3b).

Comparison of our findings with previous reports is complicated by the fact that we investigated young and healthy humans unlike most former studies, which investigated patients with cardiac disease. We found that desflurane improved $E'$, which is in contrast to previous in vitro and animal studies that found negative$^{1–7}$ or neutral effects$^{8–11}$ of all clinically used volatile anaesthetics on diastolic function. In addition, a human in vivo study found that desflurane caused impaired diastolic relaxation in subjects with CAD.$^{12}$ Also, our finding of maintained $E'$ during isoflurane anaesthesia is in contrast to impaired early diastolic function in subjects with CAD.$^{13}$ The slightly decreased $E'$ during sevoflurane anaesthesia is in agreement with a previous study in subjects with CAD$^{12}$ and similar to our previous study in young healthy subjects,$^{15}$ although the use of TTE at baseline vs transoesophageal echocardiography during mechanical ventilation in that previous study prohibited strong conclusions. Differences in the patients investigated, in the techniques used for the assessment of diastolic function, and the fact that subjects in previous studies were mechanically ventilated could have contributed to the conflicting findings. It is important to note that despite some impairment of $E'$ during mechanical ventilation in the isoflurane and sevoflurane groups, these changes were clinically irrelevant, as only one subject from the sevoflurane group showed diastolic dysfunction (i.e. $E' < 8.5 \text{ cm s}^{-1}$) and only with mechanical ventilation.

In contrast, late diastolic peak velocity of the mitral annulus $A'$—and also late transmural filling velocity $A$—similarly decreased with all three volatile anaesthetics. Decreases in $A'$ and $A$ suggest that volatile anaesthetics impair atrial systolic function causing potential impairment of late LV filling.$^{24–27}$ Missing values for FAC or ejection fraction of the left atrium preclude stronger conclusions. Nevertheless, our finding is in agreement with previous animal studies showing impaired atrial contractility with volatile anaesthetics$^{28–29}$ and a human study showing a small reduction in late transmural flow velocity induced by isoflurane and halothane.$^{31}$ A conflicting finding was reported by another human study that found no relevant impairment of atrial function by sevoflurane and desflurane in CAD patients.$^{12}$ Again, differences in the study settings and investigative techniques may have contributed to this conflicting finding.

Differences in the echocardiographic parameters of early diastolic function between spontaneous ventilation and IPPV, despite unchanged administration of volatile anaesthetics, call for critical attention. One potential confounding factor is the change in $P_{\text{a}CO_2}$ but additional factors should also be considered. A known limitation of all echocardiographic indicators of diastolic function is that they are influenced by cardiovascular factors other than diastole, most notably loading conditions and systolic functions of the ventricle and the atrium.$^{30}$ All of these factors are directly influenced by the volatile anaesthetics themselves,$^{31}$ and addition of IPPV induces further marked changes despite the absence of muscle relaxation. Despite these confounding factors, the present study provides valid information because the effects of the three volatile anaesthetics on haemodynamics, atrial and ventricular systolic function, $P_{\text{a}CO_2}$, and depth of anaesthesia did not differ. Loading conditions, as assessed by $E/E'$ and EDA, were similar between all three volatile anaesthetics, and $E/E'$ remained unchanged during all study steps. As tidal volumes applied during mechanical ventilation were weight-adjusted, it can be inferred that positive intrathoracic pressures were comparable in all groups.

Our findings of differential effects by volatile anaesthetics on early diastolic function are in agreement with a canine model of heart failure showing that desflurane better preserves diastolic function compared with sevoflurane.$^{11}$ Sympathoadrenergic effects of desflurane and sevoflurane could have resulted in better diastolic performance compared with sevoflurane. However, we did not find differences in arterial pressure and heart rate between the study groups, which questions distinct differences in sympathetic stimulation. It remains questionable whether these slight differences in $E'$ reflect differential effects of the three volatile anaesthetics on diastolic function or rather slightly differential effects on confounding factors in both the present and the former studies.$^{11}$ Moreover, the fact that $E'$, an established echocardiographic indicator of diastolic relaxation,$^{20}$ was within the normal range at all study steps in the desflurane and isoflurane groups strongly indicates that these volatile anaesthetics have no direct effect on early diastolic function, that is, relaxation. In addition, the fact that $E'$ was within the normal range in 39/40 study steps in the sevoflurane group suggests that sevoflurane might not have a clinically relevant direct effect on early diastolic function in healthy individuals. However, atrial systolic function—and, therefore, most probably late diastolic filling—was similarly impaired by all volatile anaesthetics independent of mechanical ventilation. This effect may become clinically relevant in patients with pre-existing diastolic dysfunction, for example, patients who depend on atrial contraction during LV filling.

A limitation of our study is that we did not apply invasive methods for evaluation of haemodynamics, loading, ventricular stiffness, atrial filling pressures, and diastolic function. However, although the echocardiographic methods used in our study for evaluation of in vivo heart function have limitations, these methods represent current state-of-art techniques for the non-invasive evaluation of haemodynamics, and LV systolic and diastolic function in humans.$^{18–20}$ It has been demonstrated that there is a good correlation between echocardiographic parameters and invasively evaluated parameters, and that the echocardiographic parameters...
are useful in the clinical setting. In addition, the findings assessed by tissue Doppler imaging and conventional Doppler measurement were similar. Another limitation is that the effects of the three volatile anaesthetics could not be studied during spontaneous respiration and normocapnia, because volatile anaesthesia in spontaneously breathing patients always induces hypercapnia. It seems reasonable that similar degrees of hypercapnia induced by the three anaesthetics resulted in similar confounding effects on the cardiovascular system. However, because volatile anaesthesia is used most frequently with assisted or mechanical ventilation, the measurements were repeated during step II, for example, normalized $P_a^{\text{CO}_2}$, during IPPV, but unchanged dosage of the volatile anaesthetics. The influence of $P_a^{\text{CO}_2}$ on diastolic function still has to be determined by further studies. In a canine model, high or low $P_a^{\text{CO}_2}$ did not influence myocardial contractility and LV end-diastolic pressure, but altered peripheral systemic vascular resistance, providing some evidence for no direct influence on diastolic function. A further limitation is the fixed, not random, order of the study steps I and II. However, because of the physical properties of the anaesthetics and the continuous monitoring of the end-tidal concentration of them, a relevant accumulation of the drugs in the cardiac tissue seems unlikely. Finally, the study protocol did not include a dose–response evaluation, because such evaluations frequently resulted in hypotension in a previous study when the inhalation anaesthetic was increased to $>1$ MAC, requiring administration of vasoconstrictors or even premature termination of the study. Owing to safety concerns and because administration of vasoconstrictors may confound the results, we abstained from doing dose–response investigations in the present study.

In summary, using tissue Doppler parameters of diastolic function, we found that desflurane and isoflurane, and most likely sevoflurane, have no clinically relevant negative effect on early diastolic relaxation in young subjects without cardiovascular disease. In contrast, volatile anaesthetics appear to decrease global atrial function, thereby potentially impairing late diastolic LV filling. The findings of this study cannot be directly transferred to patients with pre-existing diastolic dysfunction. Therefore, further studies investigating the effects of volatile anaesthetics in this patient population under controlled conditions are warranted.

Acknowledgements
The authors thank Claudia Werner, RN, and Esther Seeberger, RN, Department of Anaesthesia and Intensive Care Medicine, University Hospital Basel, for help with data acquisition, and Allison Dwilecki, BS, Department of Anaesthesia and Intensive Care Medicine, University Hospital Basel, Basel, Switzerland, for editorial assistance.

Conflict of interest
None declared.

Funding
This study was supported, in part, by grants from the Swiss National Science Foundation, Bern, Switzerland (Grant No. 3200B0-116229), from the European Association of Cardiothoracic Anaesthesiologists (2007 Research Grant to D.B.), and by an unrestricted research grant from Abbott AG, Switzerland. In addition, Baxter AG, Switzerland, provided the desflurane. The sponsors had no role in the design and conduct of this investigator-initiated study, in the collection, management, analysis, and interpretation of the data, or in the preparation, review, and approval of the manuscript.

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