

# Remifentanyl does not impair left ventricular systolic and diastolic function in young healthy patients

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## Editor's key points

- Opioids including remifentanyl may directly influence myocardial performance, but *in vivo* data on the effect of remifentanyl on myocardial function in humans are scarce.
- In this echocardiographic study in young healthy subjects, a continuous infusion of remifentanyl at a target concentration of 2 ng ml<sup>-1</sup> did not affect systolic and diastolic LV function.
- Further studies investigating higher concentrations of remifentanyl and patients with pre-existing cardiac diseases are needed.

**Background.** Experimental studies and investigations in patients with cardiac diseases suggest that opioids at clinical concentrations have no important direct effect on myocardial relaxation and contractility. *In vivo* data on the effect of remifentanyl on myocardial function in humans are scarce. This study aimed to investigate the effects of remifentanyl on left ventricular (LV) function in young healthy humans by transthoracic echocardiography (TTE). We hypothesized that remifentanyl does not impair systolic, diastolic LV function, or both.

**Methods.** Twelve individuals (aged 18–48 yr) without any history or signs of cardiovascular disease and undergoing minor surgical procedures under general anaesthesia were studied. Echocardiographic examinations were performed in the spontaneously breathing subjects before (baseline) and during administration of remifentanyl at a target effect-site concentration of 2 ng ml<sup>-1</sup> by target-controlled infusion. Analysis of systolic function focused on fractional area change (FAC). Analysis of diastolic function focused on peak early diastolic velocity of the mitral annulus (*e'*) and on transmitral peak flow velocity (*E*).

**Results.** Remifentanyl infusion at a target concentration of 2 ng ml<sup>-1</sup> did not affect heart rate or arterial pressure. There was no evidence of systolic or diastolic dysfunction during remifentanyl infusion, as the echocardiographic measure of systolic function (FAC) was similar to baseline, and measures of diastolic function remained unchanged (*e'*) or improved slightly (*E*).

**Conclusion.** Continuous infusion of remifentanyl in a clinically relevant concentration did not affect systolic and diastolic LV function in young healthy subjects during spontaneous breathing as indicated by TTE.

**Keywords:** analgesics opioid, remifentanyl; heart, myocardial function; monitoring, echocardiography

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Opioids are often used for induction and maintenance of anaesthesia or for sedation in patients at cardiovascular risk on intensive care units, as they are thought to have few haemodynamic side-effects and are claimed to be cardioprotective.<sup>1–2</sup> Remifentanyl is a newer potent opioid with several distinctive pharmacokinetic properties including short half-life, due to a unique metabolism by plasma and tissue esterase, and potency similar to fentanyl.<sup>3</sup> Remifentanyl has been reported to decrease both heart rate and arterial pressure during general anaesthesia, which may cause severe cardiovascular instability in some cases.<sup>4–7</sup> It may affect haemodynamic variables by histamine release or by inhibitory actions on the autonomous and central nervous systems resulting in vasodilation and bradycardia.<sup>5–9</sup> In

addition, experimental studies indicate that cardiomyocytes are regulated by opioid receptors ( $\mu$ ,  $\delta$ ,  $\kappa$ ). Opioid receptor stimulation causes direct and indirect functional changes in the heart and in myocytes.<sup>10–12</sup> Therefore, it seems reasonable to speculate that remifentanyl influences systolic and diastolic left ventricular (LV) function. *In vitro* studies on human and animal heart tissue have given conflicting results regarding a direct myocardial effect of different opioids. Fentanyl has been shown to decrease myocardial contractility of isolated rat ventricular myocytes and isolated human heart tissue,<sup>13–14</sup> whereas in other *in vitro* studies, different opioids including fentanyl, sufentanyl, and remifentanyl did not directly impair inotropic and lusitropic properties of both isolated human and perfused rabbit heart tissue.<sup>15–16</sup>

Differences in species,<sup>10</sup> study design, and drug concentrations may have contributed to the differences between studies.

Although the clinical relevance of experimental studies is acknowledged, it is important that these are supported by direct investigations of the effects of opioids on cardiac function in humans *in vivo*. The aim of this study was to investigate the effects of a clinically relevant concentration of remifentanyl on systolic and diastolic LV function in young healthy individuals. We hypothesized that remifentanyl at a target effect-site concentration of 2 ng ml<sup>-1</sup><sup>17</sup> would not impair systolic and diastolic LV function as assessed by transthoracic echocardiography (TTE).

## Methods

### Patients

After approval by the local ethics committee (Ethikkommission beider Basel, Basel, Switzerland) and obtaining written informed consent, 12 individuals (Table 1) undergoing minor surgical procedures under general anaesthesia were enrolled. 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<sup>-2</sup>. No premedication was given.

After arrival in the preoperative area, i.v. access was established and Ringer's lactate administered to replace the fluid deficit caused by overnight fasting. The deficit per hour of fasting was calculated as follows: 4 ml kg<sup>-1</sup> h<sup>-1</sup> for the first 10 kg of body weight, 2 ml kg<sup>-1</sup> h<sup>-1</sup> for the second 10 kg, and 1 ml kg<sup>-1</sup> h<sup>-1</sup> for every additional kilogram. Fifty per cent of the deficit was replaced before the start of the study. To minimize nausea and vomiting, 4 mg of tropisetron (Navoban®, Novartis Pharma, Basel, Switzerland) was given to each patient as soon as i.v. access had been established. Two-lead electrocardiogram with leads II and V5 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, bispectral index

(BIS™; Aspect 1000™, Aspect Medical Systems Inc., Natick, MA, USA; software version 1.01) was monitored continuously. Body temperature was measured continuously and kept above 36°C. Hyper- and hypotension, defined as increase and decrease of >30% from baseline value in mean arterial pressure, respectively, were treated with i.v. boluses of glyceryl trinitrate (25–50 µg) and phenylephrine (25–50 µg). Mild tachycardia or bradycardia was not treated, but the study was continued only if the heart rate recovered to values between 50 and 90 beats min<sup>-1</sup>.

The first (baseline) TTE was performed with the patient awake and unpremedicated in a partial left lateral position to optimize imaging quality. This position was maintained until the study was finished. After completion of the baseline TTE, the patient was given oxygen 2–4 litre min<sup>-1</sup> by a face mask, and an i.v. infusion of remifentanyl (Ultiva®, GlaxoSmithKline, London, UK) delivered by a target-controlled infusion system (Orchestra® Base Primera, Fresenius Vial, Brezins, France) was started. Target concentration of remifentanyl was increased stepwise by 0.5 ng ml<sup>-1</sup>. The second TTE was performed as soon as a calculated remifentanyl target concentration of 2.0 ng ml<sup>-1</sup><sup>17</sup> (corresponding to an infusion rate of 0.08–0.09 µg kg<sup>-1</sup> min<sup>-1</sup>) and stable haemodynamics had been reached. Stable haemodynamics were predefined as <5% variation of mean arterial pressure and heart rate over three consecutive measurements performed within 6 min. When the second TTE was finished, the study protocol was completed.

### Doppler echocardiography

All echocardiograms were obtained with a Sonos™ 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.<sup>18 19</sup> The echocardiographic data were digitally stored for subsequent off-line analysis. All TTE examinations were performed by the same operator. Standard LV short-axis and two- and four-chamber views were obtained from the parasternal and apical views. For the pulsed-wave Doppler recordings of the mitral inflow, the sample volume was positioned between the tips of the open mitral leaflets using optimal alignment with transmitral blood flow. For recordings of isovolumic relaxation time (IVRT), the beam was slightly moved towards the LV outflow tract to obtain recordings of both LV inflow and LV outflow signals. For recordings of pulsed-wave tissue Doppler imaging, the sample volume was placed at the septal and lateral sides of the mitral annulus, and the acoustic power and the filter frequencies of the system were set to the lowest possible values. The following variables were measured: end-diastolic and end-systolic areas (EDA and ESA, respectively), peak early and peak late transmitral filling velocities (E and A, respectively), deceleration time (DT), IVRT, early and late diastolic velocities (e' and a', respectively), and peak systolic velocity (s') of the mitral annulus predefined as the average of the septal and lateral mitral annulus measurements obtained by tissue Doppler

**Table 1** Patient characteristics. Values are expressed as numbers (%) or median (range). ASA, American Society of Anesthesiology Risk Index; BMI, body mass index

	Study patients (n=12)
ASA class I	12 (100)
Women	7 (58)
Age (yr)	26 (19–45)
Weight (kg)	64 (55–85)
Height (cm)	169 (163–181)
BMI (kg m <sup>-2</sup> )	22 (20–26)
Haemoglobin (g litre <sup>-1</sup> )	142 (121–152)
Haematocrit (%)	40 (35–45)
Creatinine (µmol litre <sup>-1</sup> )	63 (47–94)

imaging. The following derived variables were calculated from these data: fractional area change (FAC)=[(EDA–ESA)/EDA]×100, ratio  $E/A$ , ratio  $E/e'$ , and ratio  $e'/a'$ . In addition, we determined the myocardial performance index (MPI) as a measure of global cardiac function. This index, defined as the sum of isovolumic contraction and relaxation time divided by the ejection time, was reported by Tei and colleagues<sup>20</sup> to be a simple and reproducible indicator of cardiac function and to be independent of heart rate and arterial pressure. LV preload was estimated by EDA and  $E/e'$  ratio (which reflects LV filling pressure); LV afterload was assessed by the end-systolic arterial pressure–area product (SAP×ESA).<sup>21</sup>

Analysis of systolic function focused on FAC, and analysis of diastolic function focused on  $e'$  and  $E$ . FAC correlates well with LV ejection fraction;<sup>22</sup>  $E$  and  $e'$  reflect the early diastolic filling which depends on the pressure gradient between the atrium and ventricle, LV myocardial relaxation, and early diastolic untwisting.<sup>19</sup>

All variables were measured at end-expiration over three preferably consecutive cardiac cycles and averaged by one experienced physician-echocardiographer not involved in data acquisition and blinded to all other study data. In a previous study from our group with a similar setting, intra- and inter-observer variability (calculated as the mean absolute difference between two readings divided by their mean and expressed as percentage) were 1.5–4.2% and 2.6–6.9%, respectively.<sup>23</sup> In the present study, we did not re-evaluate inter- and intra-observer variability.

### Statistical analysis

The sample size calculation was based on our previous study<sup>24</sup> estimating that a size of 12 patients would allow to detect an increase or decrease in  $e'$  or FAC of 20% by the Wilcoxon signed-rank test ( $\alpha < 0.05$  and  $\beta \geq 0.8$ ).

Data are presented as median (range) or number (percentage) where appropriate. Comparisons for the haemodynamic and echocardiographic effects caused by remifentanil were performed by the two-tailed Wilcoxon signed-rank test. A  $P$ -value of  $< 0.05$  was considered statistically significant. All statistical analyses were performed using an SPSS for Windows 16.0 computer package (SPSS Inc., Chicago, IL, USA).

### Results

The study was safely performed in all patients. No complications occurred during or after the study. No patient showed signs of relevant muscle rigidity or upper airway obstruction during remifentanil infusion. No patient reported nausea. Patients were conscious during the study but became obviously sedated by remifentanil at an end-organ concentration of 2 ng ml<sup>-1</sup>. However, this observation was not reflected by decreased BIS values.

No medication to increase or decrease arterial pressure or heart rate was administered during the study, as arterial

pressure and heart rate did not markedly change during remifentanil infusion (Table 2).

### Effects of remifentanil on LV systolic function

At baseline, systolic function was normal in all patients: FAC was  $\geq 52\%$ ,<sup>22</sup>  $MPI \leq 0.33$ ,<sup>20</sup> and  $s' \geq 8.2$  cm s<sup>-1</sup> in each patient.<sup>25</sup> Remifentanil at a target concentration of 2 ng ml<sup>-1</sup> did not change the measured echocardiographic indices of systolic function, that is, FAC, MPI, and  $s'$  were similar to baseline values (Table 3).

### Effects of remifentanil on LV diastolic function

At baseline, there were no signs of diastolic dysfunction:  $e'$  was  $\geq 12.0$  cm s<sup>-1</sup>,  $E \geq 64$  cm s<sup>-1</sup>, and  $E/A$  ratio  $\geq 1.3$  in each patient.<sup>19</sup> Remifentanil at a target concentration of 2 ng ml<sup>-1</sup> did not induce any echocardiographic signs of diastolic dysfunction, i.e.  $e'$  was similar to baseline ( $P=0.31$ ), and  $E$  and the  $E/A$  ratio were slightly increased ( $P=0.02$  and 0.03, respectively).

### Effects of remifentanil on LV preload and afterload

Regarding the echocardiographic indices of LV filling, there was a slight increase in EDA ( $P=0.03$ ) but only a trend towards an increased  $E/e'$  ratio ( $P=0.06$ ), which better reflects LV filling pressure (Table 3).<sup>19</sup> There was no difference in the end-systolic arterial pressure–area product before and during remifentanil infusion ( $P=0.21$ ).

### Discussion

Our study found that remifentanil at a clinically relevant infusion rate of 0.08–0.09  $\mu\text{g kg}^{-1} \text{min}^{-1}$  did not impair systolic and diastolic LV function in spontaneously breathing healthy young surgical patients with normal heart function. The echocardiographic indices of systolic function, that is, FAC and  $s'$ , were not affected by remifentanil. In contrast, the indices of diastolic function were slightly changed during remifentanil infusion with small but statistically significant increases in  $E$  and  $E/A$  ratio. However, the lack of any effect

**Table 2** Physiological variables at baseline and during remifentanil infusion in the 12 study patients. Values are expressed as median (range).  $P$ -values were calculated by the Wilcoxon signed-rank test

	Baseline	Remifentanil	$P$ -value
Systolic arterial pressure (mm Hg)	119 (97–145)	121 (100–146)	0.12
Mean arterial pressure (mm Hg)	79 (67–98)	82 (69–99)	0.27
Diastolic arterial pressure (mm Hg)	59 (51–75)	62 (52–76)	0.18
Heart rate (beats min <sup>-1</sup> )	60 (46–98)	61 (42–83)	0.16
O <sub>2</sub> saturation (%)	98 (94–99)	99 (98–100)	0.01
Bispectral index	96 (90–98)	96 (92–98)	0.29

**Table 3** Echocardiographic variables at baseline and during remifentanyl infusion in the 12 study patients, and reported normal values of these variables in healthy, awake subjects aged 20–40 yr.<sup>19 20 23 43</sup> \*Study data are expressed as median (range). P-values were calculated by the Wilcoxon signed-rank test. †Normal values are expressed as mean (sd). N/A, not available

	Baseline*	Remifentanyl*	P-value	Normal values†
Peak early transmitral filling velocity, E (cm s <sup>-1</sup> )	89 (63–117)	95 (75–114)	0.02	76 (15)
Peak late transmitral filling velocity, A (cm s <sup>-1</sup> )	52 (29–74)	52 (33–71)	0.53	44 (14)
Ratio E/A	1.6 (1.3–2.5)	2.0 (1.4–3.0)	0.03	1.8 (0.6)
Peak early mitral diastolic annular velocity, e' (cm s <sup>-1</sup> )	14.8 (12.0–20.4)	15.1 (12.7–21.4)	0.31	14.1 (2.7)
Peak late mitral diastolic annular velocity, a' (cm s <sup>-1</sup> )	8.1 (5.6–12.5)	8.6 (4.7–11.6)	0.53	9.1 (1.7)
Ratio e'/a'	2.0 (1.1–3.0)	1.9 (1.2–3.2)	0.39	1.8 (0.6)
Ratio E/e'	5.8 (4.0–7.3)	6.8 (4.6–7.6)	0.06	5.6 (1.3)
Deceleration time, DT (ms)	189 (153–263)	177 (148–257)	0.17	217 (65)
Isovolumic relaxation time, IVRT (ms)	59 (42–93)	52 (37–85)	0.07	91 (17)
Peak systolic mitral annular velocity, s' (cm s <sup>-1</sup> )	10.3 (8.2–11.7)	10.4 (7.6–12.2)	0.53	9.4 (1.4)
End-diastolic area, EDA (cm <sup>2</sup> )	16.6 (12.5–21.6)	17.2 (13.9–23.3)	0.03	18.8 (1.4)
End-systolic area, ESA (cm <sup>2</sup> )	7.5 (4.4–10.4)	7.3 (5.1–10.7)	0.30	8.5 (2.0)
Fractional area change, FAC (%)	56 (52–65)	58 (52–63)	0.37	56 (5)
End-systolic arterial pressure–area product, SAP×ESA (mm Hg cm <sup>2</sup> )	818 (540–1298)	836 (631–1293)	0.21	N/A
Myocardial performance index, MPI	0.23 (0.09–0.33)	0.20 (0.09–0.28)	0.24	0.36 (0.10)

on e' calls into question the interpretation of these changes as being indicative of improved early diastolic function. Preload was only minimally affected by remifentanyl, as indicated by slightly increased EDA but insignificantly increased E/e' ratio. Afterload remained similar to baseline during remifentanyl infusion, as indicated by the unchanged end-systolic pressure–area product. As our study was powered to assess changes in e' and FAC as main diastolic and systolic variables, differences in other echocardiographic indices must be interpreted cautiously.

Comparison of our findings with previous reports is complicated by several facts. First, most previous studies investigated the effects of remifentanyl in experimental designs using human and animal heart tissue rather than *in vivo*.<sup>14–16</sup> Secondly, to our knowledge, modern echocardiographic techniques have not previously been used to evaluate the effects of opioids on diastolic and systolic cardiac function in adults. An echocardiographic study in children anaesthetized with sevoflurane showed a decreased cardiac output by the addition of remifentanyl, mainly as a result of a decrease in heart rate.<sup>9</sup> Another echocardiographic study from 1986 using the inferior M-mode technique showed that naloxone, an opioid antagonist, did not affect cardiac dimension and function in healthy adult subjects.<sup>26</sup> Thirdly, former *in vivo* studies investigated patients with cardiac diseases and impaired heart function or critically ill patients.<sup>5 7–8 27 28</sup> However, in agreement with our results, remifentanyl did not impair systolic and diastolic properties of myocardial tissue and of isolated rabbit hearts in two experimental studies.<sup>15</sup> <sup>16</sup> Also, in support of our findings is the fact that remifentanyl has been successfully used as an anaesthetic agent in high-risk patients undergoing cardiac surgery, implantation of cardiac defibrillators, and Caesarean section in the presence of peripartur cardiomyopathy.<sup>7 29 30</sup> These investigations and

reports showed that remifentanyl provides stable haemodynamic conditions even in patients with severely impaired cardiac function.

Conflicting findings have been reported by several studies. A porcine study found that remifentanyl directly affects the sinus node,<sup>31</sup> thereby inducing bradycardia. Other experimental studies found that remifentanyl has a vasorelaxant effect on human saphenous veins<sup>14</sup> and radial arteries.<sup>32</sup> Several human studies on remifentanyl found cardiovascular side-effects including severe bradycardia and hypotension due to vasodilation.<sup>4–9</sup> In patients with total artificial hearts, remifentanyl induced a dose-dependent decrease in systemic arterial pressure and a decreased resistance in arterial vessels but not in veins.<sup>8</sup>

There are several reasons that may explain the conflicting findings including differences in the patient population,<sup>8 11 12</sup> the study protocol,<sup>13 14</sup> and the species.<sup>10 13 16</sup> For example, the effects of remifentanyl on myocardial function and haemodynamics in healthy individuals with normal heart function, as in our study, may differ from those in critically ill or cardiac patients.<sup>7 8 11 12</sup> Another reason for differences between the studies is that hypotension and bradycardia seem to be particularly pronounced when a high dose or bolus of remifentanyl is administered, or during co-administration of remifentanyl together with propofol or other anaesthetics during the induction of anaesthesia.<sup>5 9</sup> In our study, we did not administer remifentanyl at a high dose and administered it as the sole drug. Another reason for conflicting results is the use of neuromuscular blocking agents and intermittent positive pressure ventilation in several other studies in anaesthetized patients,<sup>5 7 8</sup> which both may affect cardiac function by affecting preload and afterload.<sup>24 33</sup> Taken together, the results from our study and former *in vitro* and *in vivo* studies and also case reports



suggest that remifentanyl at a low-dose infusion rate does not relevantly impair myocardial systolic, diastolic LV function, or both. However, cardiovascular side-effects may become evident with remifentanyl bolus administration or infusion at high dose or when co-administrated with propofol or sevoflurane.<sup>5-9</sup>

Besides a pronounced analgesic effect, all opioids also provide dosage-related sedative effects. During remifentanyl infusion in this study, patients became sedated but all patients remained conscious and BIS values were unaffected. Previous studies investigating the effect of remifentanyl on BIS values have yielded controversial results,<sup>6, 34, 35</sup> but the comparison with our data is complicated by the fact that in those studies remifentanyl was administered in critically ill patients<sup>27</sup> or co-administered with other sedatives.<sup>6, 34, 35</sup> As we did not formally assess depth of sedation, conclusions about the effect of the depth of sedation on cardiac performance are not possible from our data.

Our study has several limitations. First, the study protocol did not include a dose–response evaluation. Safety concerns regarding adequate respiratory drive in spontaneously breathing patients<sup>27</sup> and regarding haemodynamic stability<sup>4-7</sup> kept us from administering high concentrations of remifentanyl requiring tracheal intubation and the administration of other medication that would potentially influence cardiac function. The investigated target concentration of 2 ng ml<sup>-1</sup> corresponds to remifentanyl infusion rates that have been used safely during surgical procedures,<sup>36, 37</sup> for sedation on the intensive care unit,<sup>27, 28</sup> or for early post-operative analgesia.<sup>38</sup> Therefore, the present study gives clinically important information on the effects of remifentanyl on LV function at a lower dose but cannot exclude different effects at a higher dose, or after combined administration of remifentanyl together with other analgesic or anaesthetic drugs. In addition, no conclusions must be drawn from our findings with remifentanyl to the effects of other opioids.

Secondly, spontaneous breathing during remifentanyl infusion and oxygen supplementation might result in elevated concentrations of  $P_{aCO_2}$  and  $P_{aO_2}$ . Hypercapnia is known to decrease systemic vascular resistance and increase stroke volume and cardiac output,<sup>39, 40</sup> whereas hyperoxaemia may increase systemic vascular resistance.<sup>41</sup> Therefore, both increased concentration of  $P_{aCO_2}$  and  $P_{aO_2}$  may potentially influence LV filling and consequently LV function. However, remifentanyl infusion up to 0.1 µg kg<sup>-1</sup> min<sup>-1</sup> in spontaneously breathing critically ill patients did not result in a suppression of respiratory drive or in a relevant increase in  $P_{aCO_2}$ .<sup>27</sup> The use of an even lower remifentanyl concentration in our study suggests unchanged  $P_{aCO_2}$  concentrations in our patients, but we do not have measurements to confirm this. Therefore, we cannot fully exclude an increase in  $P_{aCO_2}$  in our patients during remifentanyl administration. Changes in  $P_{aCO_2}$  and  $P_{aO_2}$  are unlikely to be confounders in our study, because previous studies have found that  $P_{aCO_2}$  did not relevantly impair diastolic and systolic function<sup>23, 40</sup> and that  $P_{aO_2}$  may only affect cardiac function at very high levels.<sup>41</sup>

Thirdly, we applied a standardized infusion therapy but could not strictly control preload and afterload, both of which may influence echocardiographic indicators of systolic and diastolic function.<sup>42</sup> However, stable haemodynamics and unchanged intracardiac pressures, as indicated by the  $E/e'$  ratio and the end-systolic pressure–area product, strongly suggest that there were no relevant changes in preload and afterload that might have confounded our results.

Finally, it must be noted that we did not measure remifentanyl plasma concentrations. We used a commercially available and widely used calculated pharmacokinetic model taking into account patient's age, weight, height, and gender.<sup>17</sup> A previous study using a similar computerized program showed that the difference between calculated and measured remifentanyl plasma concentrations may be substantial at target concentrations  $\geq 5$  ng ml<sup>-1</sup> but much smaller at the concentration used in the present study.<sup>6</sup> However, we cannot completely exclude potentially substantial differences between calculated and existing remifentanyl concentrations in our study patients, as we did not measure plasma concentrations.

In conclusion, the present study found that remifentanyl at a calculated target effect-site concentration of 2 ng ml<sup>-1</sup> did not impair systolic or diastolic cardiac function in young surgical patients free from cardiac disease. These results support previous data suggesting that remifentanyl at a low dose is a suitable drug for sedation in patients with normal heart function undergoing monitored anaesthesia care or on intensive care units. Further studies in patients at cardiac risk are needed before such a conclusion is extended to patients with pre-existing cardiac disease.

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## Conflict of interest

None declared.

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