## Lung function after total intravenous anaesthesia or balanced anaesthesia with sevoflurane

W. Tiefenthaler<sup>1</sup>, D. Pehboeck<sup>1\*</sup>, E. Hammerle<sup>1</sup>, P. Kavakebi<sup>2</sup> and A. Benzer<sup>1</sup>

<sup>1</sup> Department of Anaesthesiology and Critical Care Medicine and <sup>2</sup> Department of Neurosurgery, Innsbruck Medical University, Anichstrasse 35, 6020 Innsbruck, Austria

\* Corresponding author. E-mail: daniel.pehboeck@uki.at

#### **Editor's key points**

- Earlier work found a decrease in respiratory parameters in the immediate postoperative period after general and regional anaesthesia.
- In this study, irrespective of the type of anaesthesia administered, lung function parameters decreased after operation.
- Postoperative decrease in forced vital capacity was greater after total i.v. anaesthesia than after balanced anaesthesia with sevoflurane.

**Background**. We investigated the effects of total i.v. anaesthesia (TIVA) and balanced anaesthesia (BAL) with sevoflurane on postoperative lung function in patients undergoing surgery in the prone position.

**Methods.** Sixty patients, aged 21–60 yr, undergoing elective lumbar disc surgery in the prone position were randomly allocated to undergo TIVA (propofol-remifentanil) or BAL (fentanyl-nitrous oxide-sevoflurane). Forced vital capacity (FVC), forced expiratory volume in 1 s, mid-expiratory flow (MEF 25–75), and peak expiratory flow were measured before and after general anaesthesia.

**Results.** Both groups were similar with respect to patient characteristic data and preoperative lung function parameters. Irrespective of the type of anaesthesia administered, lung function parameters decreased after operation, with the decrease in FVC being greater after TIVA than after BAL with sevoflurane.

**Conclusions.** In patients emerging from general anaesthesia, postoperative reduction in FVC is greater after TIVA than after BAL with sevoflurane.

**Keywords:** anaesthesia, general; anaesthetic techniques, inhalation; anaesthetic techniques, i.v.; monitoring, spirometry

Accepted for publication: 25 August 2010

After awakening from general anaesthesia, patients regularly show a more or less strongly pronounced impairment of lung function. Such a decrease in respiratory parameters in the immediate postoperative period has been found after general and regional anaesthesia,<sup>1 2</sup> in patients after intra-abdominal or superficial surgery<sup>3</sup> and in normal weight and overweight patients.<sup>4</sup>

Although von Ungern-Sternberg and colleagues already showed that the decrease in postoperative lung function is significantly smaller after spinal anaesthesia than after general anaesthesia,<sup>5</sup> studies are lacking on possible other effects of balanced anaesthesia (BAL) or total i.v. anaesthesia (TIVA) on postoperative lung function. The choice of various anaesthesia procedures (i.e. TIVA, BAL) is made largely on the basis of the anaesthetist's personal experience and expertise with the particular procedure. Many anaesthetists use BAL techniques with halogenated anaesthetics, that is, because of their bronchodilatory effects<sup>5</sup> and the low risk of awareness,<sup>6</sup> whereas the advantages of TIVA are, for example, that it is easy to control and has shorter recovery times.<sup>7</sup>

Whether the known negative effects of a general anaesthesia on lung function affect all parameters to the same extent, or whether various parameters are affected differently by BAL or TIVA, has not yet been investigated. For this reason, we aimed in the current study to detect such a possible different influence on the part of TIVA or BAL with sevoflurane on the various postoperative lung function parameters in patients undergoing general anaesthesia in the prone position.

#### Methods

#### **Study population**

After institutional ethics committee approval, 60 patients (ASA I–II) undergoing lumbar disc surgery in the prone position were enrolled after giving written informed consent. Exclusion criteria included diagnosed obstructive sleep apnoea syndrome, significant cardiopulmonary disease, morbid obesity, patients with compromised liver and kidney functions, or neurological disorders.

#### General anaesthesia

No premedication was given before anaesthesia. Routine anaesthesia monitoring consisted of ECG, pulse oximetry, non-invasive arterial pressure at 3 min intervals, capnography, end-tidal concentration of volatile anaesthetics, and train-of-four (TOF) monitoring (Datex Engstrom AS/3 Anaesthesia Monitor; Helsinki, Finland). After random allocation

© The Author [2010]. Published by Oxford University Press on behalf of the British Journal of Anaesthesia. All rights reserved. For Permissions, please email: journals.permissions@oxfordjournal.org

according to a randomization list, patients received either remifentanil 1  $\mu$ g kg<sup>-1</sup> (TIVA group) or fentanyl 3  $\mu$ g kg<sup>-1</sup> (BAL group), and anaesthesia was induced with propofol 2.5 mg kg<sup>-1</sup> followed by rocuronium 0.6 mg kg<sup>-1</sup> after loss of consciousness. Tracheal intubation was performed under the direct laryngoscopic view by a consultant. We used tracheal tubes with high-volume, low-pressure cuffs, 7.5 mm internal diameter for women and 8.5 mm internal diameter for men (Mallinckrodt Inc., St Louis, MO, USA). The cuff was inflated with air, and cuff pressure was monitored and maintained at 20 mbar throughout the procedure. Anaesthesia was maintained either with remifertanil 0.25  $\mu$ g kg<sup>-1</sup> min<sup>-1</sup> and propofol 100  $\mu$ g kg<sup>-1</sup> min<sup>-1</sup> and an air/oxygen mixture (TIVA group), or with sevoflurane 2 vol% and nitrous oxide 70% in oxygen (BAL group). Controlled ventilation was adjusted to end-tidal CO<sub>2</sub> of 4.6 (sp 0.5) kPa. The patient was placed in the prone position on a Wilson frame. Fifteen minutes before the end of surgery, all patients received diclofenac 75 mg for postoperative analgesia. Extubation was performed at an O<sub>2</sub> concentration of 80%.<sup>8</sup> Return of neuromuscular function was confirmed using TOF peripheral nerve stimulation. In the case of residual block, neostigmine and alycopyrrolate were administered. Before extubation, four equal twitches in the TOF without tetanic fade (50 Hz over 5 s) were required (GE Healthcare Finland Oy Helsinki Type E-NMT-00). After surgery was completed, anaesthetic agents (sevoflurane or remifentanil/propofol) were discontinued. After resumption of spontaneous ventilation, the trachea was extubated while applying suction through the tube when patients opened their eyes, lifted their head, or attempted self-extubation. After extubation, the patient was directly transferred from the knee-elbow position to a bed. Any episode of bronchospasm, laryngospasm, or desaturation (Sp $_{O_2}$  <95%), and also the duration of surgery, was recorded.

#### Spirometry

On arrival in the operating area before surgery, a baseline spirometry (SPIRO preoperative) measurement was taken after a thorough demonstration of the correct usage. Spirometry was standardized with each patient in a  $30^{\circ}$  head-up position.

Forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1), mid-expiratory flow (MEF 25–75), and peak expiratory flow (PEF) were measured. At each assessment time, spirometry was performed at least three times to be able to meet the criteria of the European Respiratory Society (ERS); the best measurement was recorded.

After surgery, the patient was discharged to the postanesthesia care unit (PACU). Pain was assessed using visual analogue scale (VAS) and, if necessary, analgesic therapy performed. In both groups, postoperative basic analgesia consisted of paracetamol 1000 mg i.v. and diclofenac 75 mg i.v. starting directly at the end of the operation. Adequate analgesia was defined as a VAS score <3. If pain persisted in the PACU, a morphine bolus of 3 mg was given. As soon as the patient was alert and fully cooperative and VAS pain score <3, we performed spirometry for the second time (SPIRO postoperative). In each patient, pre- and postoperative spirometry was performed by the same anaesthesia care nurse trained to use the spirometer and blinded with regard to the randomization group.

#### Statistical analysis

The change between pre- and postoperative FEV1 was used to predict the sample dimension. Preliminary data indicated that a sample size of 27 in each group will have 80% power to detect a difference in means of -0.820 (difference between a Group 1 mean of 4.580 and a Group 2 mean of 5.400), assuming that the common standard deviation (sD) is 1.040 using a two-group *t*-test with 0.05 two-sided significance level. The study population was thus prospectively set at 60 patients.

The analysed data are normally distributed as evaluated by the Kolmogorov–Smirnov test. Data are shown as mean and sp. Comparisons between the groups were performed with an unpaired *t*-test for parametric data; differences between SPIRO preoperative and SPIRO postoperative in each group were tested with a paired *t*-test.

## Results

Thirty patients in the TIVA group and 30 patients in the BAL group were enrolled in the study. Except for three patients in the TIVA group and two patients in the BAL group, who were unable to completely perform pre-/postoperative pulmonary function tests and whose data were therefore excluded from analysis, all patients were able to do a complete spirometry sequence consisting of one preoperative measurement and one measurement within the first hour after extubation. No adverse events were observed in any of the patients during the study. The ratio FEV1/FVC did not change in either group throughout the study period, thereby indicating restrictive changes in lung function. No difference was found between the TIVA group and the BAL group with respect to patient characteristics, but in relation to the proportion of smokers (Table 1).

# Forced expiratory volume in 1 s, mid-expiratory flow, and peak expiratory flow

In both groups, preoperative values for FEV1, MEF 25–75, and PEF were within the normal ranges and decreased significantly after emergence from general anaesthesia when compared with preoperative values, but no difference was observed between the two groups (Table 2).

## Forced vital capacity

In both groups, baseline values were within the normal range, decreasing after anaesthesia irrespective of the type of anaesthesia (Table 2). A significantly greater decrease in FVC was observed in the TIVA group than in the BAL group (Table 2).

	TIVA group (n=27)	BAL group (n=28)		
Age (yr)	41 (21-60)	41 (24–59)		
Sex ratio (M/F)	15/ 12	22/6		
Weight (kg)	79 (12)	82 (15)		
Height (cm)	178 (8)	180 (9)		
BMI (kg m <sup><math>-2</math></sup> )	24 (3)	25 (3)		
Smokers	6 (22%)	11 (39%)		
Time of surgery (min)	97 (25)	100 (35)		
Time interval (min)				
SPIRO preoperative	158 (40)	168 (40)		
SPIRO postoperative				

 Table 1
 Patient characteristics. Data are mean (range) or mean

 (sp) or total number of patients

## Discussion

Similar to the results of previous investigations,<sup>1 2 5</sup> we found a decrease in respiratory parameters (FVC, FEV1, MEF 25–75, and PEF) in patients emerging from general anaesthesia. A new finding made in our study is that after general anaesthesia, FVC decreased less in patients after BAL with sevoflurane than in patients who had undergone TIVA.

The decrease in lung function with simultaneously unchanged FEV1/FVC ratio observed in both groups points to a restrictive disturbance in lung function, as already described in previous investigations.<sup>3 9 10</sup> Rothen and colleagues<sup>11</sup> showed that these restrictive changes are due to the development of atelectasis after induction of general anaesthesia, whereby the extent of the atelectasis in turn influences the extent to which FVC or FEV1 is reduced.<sup>12 13</sup>

Although mechanical ventilation and especially patient position (i.e. prone position) applied intraoperatively during general anaesthesia can even improve lung volumes and oxygenation of patients,<sup>14</sup> restrictive lung function disorder after general anaesthesia is a constant, reproducible finding that can be observed starting in the early publications by Diament and Palmer<sup>1</sup> right up to today in all subsequent studies.<sup>15</sup> Olimpio and colleagues<sup>16</sup> already showed that prone extubation after lumbar spine surgery is safe and offers greater haemodynamic stability and less coughing than is the case in patients extubated after returning to the spine position.<sup>17</sup> Further studies should evaluate a possible influence of the patient position (supine vs. prone) on the lung function after general anaesthesia. At our clinic, extubation after uncomplicated interventions and in the prone position has been a standard procedure for more than 20 yr and has shown excellent results. When lung function after operation begins to normalize is unclear. This is determined not only by the type of anaesthesia procedure administered, but also by the location and scope of the surgical intervention.<sup>18</sup>

The occurrence of atelectasis with subsequent changes in FVC appears to be caused by an anaesthetic-induced decrease in respiratory muscles, especially a loss of diaphragmatic tone.<sup>19</sup> The findings with regard to halogenated anaesthetics are contradictory. Although Langeron and colleagues<sup>20</sup> found no effect of isoflurane or halothane in an isolated rat diaphragm, others demonstrated a negative effect of sevoflurane on diaphragmatic contractility in dogs, predominantly of the crural part.<sup>21</sup> In a recently published study, Zhang and colleagues<sup>22</sup> found a decline in twitch diaphragmatic pressure in humans after a single bolus of propofol of 2 mg kg<sup>-1</sup>. Although Jensen and colleagues<sup>23</sup> found no difference in the scope of atelectasis after TIVA or BAL, they also did not perform spirometry in their study.

In a previous study, we found a significantly higher incidence of coughing in patients after emerging from BAl with sevoflurane than after emerging from TIVA.<sup>24</sup> As coughing is similar to a vital capacity manoeuvre (inflating the lungs to 40 cm H<sub>2</sub>O for 15 s), which has been shown to be effective in reducing the incidence of atelectasis,<sup>24</sup> it may be speculated that such an otherwise unwanted side-effect could have contributed to the better results found in the BAL patients in our study.

Moreover, volatile anaesthetics are well-known bronchodilators, in that they deplete sarcoplasmic reticulum Ca<sup>2+</sup> stores. An *in vitro* experiment showed halothane, isoflurane, and sevoflurane to prevent sarcoplasmic reticulum refilling by inhibiting store-operated Ca<sup>2+</sup> entry. Such interactions likely result in substantial airway relaxation and may help maintain anaesthetic-induced bronchodilation.<sup>25</sup>

Already clinical experience leads us to suspect that the type and location of the surgical intervention influence the changes in lung function occurring after the operation and anaesthesia. Various studies confirm that impairment of lung function is greater after intra-abdominal interventions than after peripheral surgery.<sup>3</sup> In order to minimize this surgical factor when assessing lung function, we felt that lumbar hemilaminectomy would be the typical suitable operation.

Premedication, even in small amounts, affects results of spirometry, possibly by depressing the activity of respiratory

**Table 2** Absolute and relative values for FVC, FEV1, PEF rate and MEF rate for patients before (SPIRO preoperative) or after (SPIRO postoperative) TIVA or BAL. Values are mean (sp). Significant changes within groups (+) and between groups (\*) are indicated

	FVC		FEV1		PEF		MEF 25-75	
	TIVA	BAL	TIVA	BAL	TIVA	BAL	TIVA	BAL
SPIRO preoperative	4.7 (1.1)	5.1 (0.7)	3.6 (0.9)	3.8 (0.7)	8.4 (2.1)	8.8 (1.7)	3.2 (1.2)	3.1 (1.0)
SPIRO postoperative	4.4 <sup>+,</sup> * (1.1)	4.9 <sup>+,</sup> * (0.7)	3.4+ (0.9)	3.6+ (0.6)	7.3 <sup>+</sup> (2.0)	7.6 <sup>+</sup> (1.8)	2.9 <sup>+</sup> (1.2)	2.9 <sup>+</sup> (0.9)

muscles and by exerting sedative effects.<sup>2 3 26</sup> Sedative aftereffects of general anaesthesia can also distort measurement readings, which is why we performed spirometry in our study as soon as patients were alert and cooperative.

Since postoperative pain also contributes significantly to temporary deterioration in lung function, especially vital capacity,<sup>27</sup> it was important to avoid a pain-induced influence on postoperative measurements. For this reason, spirometry was performed in our study in alert patients and when lung function reached a predefined threshold (VAS < 3) that was identical for both study groups. All patients were able to do a spirometry measurement according to the ERS criteria in the first hour after extubation. We also did not compare the requirement for postoperative analgesia/ opioids, because Gunaydin and colleagues<sup>28</sup> showed that FVC and FEV1 did not change, not even for constant opioid administration in alert patients. This is also confirmed by results reported by others,<sup>29</sup> who found no difference in postoperative lung function after desflurane/remifentanil anaesthesia or desflurane/sufentanil anaesthesia, provided that spirometry was performed at a similar VAS score after administration of various morphine doses.

In conclusion, our study confirms the results of previous investigations showing a decrease in lung function parameters after general anaesthesia, but demonstrates for the first time that in the first postoperative hour, the decrease in FVC is significantly less after BAL with sevoflurane than in patients who underwent TIVA with propofol and remifentanil. The aim of this study was to investigate the effects of general anaesthesia in patients with normal lung function. On the basis of our findings, further studies should evaluate the clinical effects of different anaesthesia regimes in patients with compromised lung function.

However, whether such reduction in FVC after TIVA should influence the clinician's decision at this time when choosing between TIVA and a BAL-specific anaesthetic technique depends on the particular clinical situation, possible other disorders, and the surgical demands.

## **Conflict of interest**

None declared.

## References

- Diament ML, Palmer KN. Postoperative changes in gas tensions of arterial blood and in ventilatory function. *Lancet* 1966; 7456: 180-2
- 2 Hedenstierna G, Löfström J. Effect of anaesthesia on respiratory function after major lower extremity surgery. A comparison between bupivacaine spinal analgesia with low-dose morphine and general anaesthesia. Acta Anaesthesiol Scand 1985; 29: 55–60
- 3 von Ungern-Sternberg BS, Regli A, Schneider MC, Kunz F, Reber A. Effect of obesity and site of surgery on perioperative lung volumes. *Br J Anaesth* 2004; **92**: 202–7
- 4 von Ungern-Sternberg BS, Regli A, Reber A, Schneider MC. Comparison of perioperative spirometric data following spinal or general anaesthesia in normal-weight and overweight gynaecological patients. *Acta Anaesthesiol Scand* 2005; **49**: 940–8

- 5 Rooke GA, Choi JH, Bishop MJ. The effect of isoflurane, halothane, sevoflurane, and thiopental/nitrous oxide on respiratory system resistance after tracheal intubation. *Anesthesiology* 1997; **86**: 1294–9
- 6 Errando CL, Sigl JC, Robles M, et al. Awareness with recall during general anaesthesia: a prospective observational evaluation of 4001 patients. Br J Anaesth 2008; **101**: 178–85
- 7 Juckenhöfel S, Feisel C, Schmitt HJ, Biedler A. TIVA with propofolremifentanil or balanced anesthesia with sevoflurane–fentanyl in laparoscopic operations. Hemodynamics, awakening and adverse effects. *Anaesthesist* 1999; **48**: 807–12
- 8 Akça O, Podolsky A, Eisenhuber E, et al. Comparable postoperative pulmonary atelectasis in patients given 30% or 80% oxygen during and 2 hours after colon resection. Anesthesiology 1999; 91: 991–8
- 9 Natalini G, Franceschetti ME, Pletti C, Recupero D, Lanza G, Bernardini A. Impact of laryngeal mask airway and tracheal tube on pulmonary function during the early postoperative period. Acta Anaesthesiol Scand 2002; **46**: 525–8
- 10 Craig DB. Postoperative recovery of pulmonary function. Anesth Analg 1981; **60**: 46–52
- 11 Rothen HU, Sporre B, Engberg G, Wegenius G, Reber A, Hedenstierna G. Prevention of atelectasis during general anaesthesia. *Lancet* 1995; **345**: 1387–91
- 12 Karayiannakis AJ, Makri GG, Mantzioka A, Karousos D, Karatzas G. Postoperative pulmonary function after laparoscopic and open cholecystectomy. Br J Anaesth 1996; 77: 448–52
- 13 Lindberg P, Gunnarsson L, Tokics L, et al. Atelectasis and lung function in the postoperative period. Acta Anaesthesiol Scand 1992; 36: 546-53
- 14 Pelosi P, Croci M, Calappi E, et al. The prone positioning during general anesthesia minimally affects respiratory mechanics while improving functional residual capacity and increasing oxygen tension. Anesth Analg 1995; **80**: 955–60
- 15 Cadi P, Guenoun T, Journois D. Pressure-controlled ventilation improves oxygenation during laparoscopic obesity surgery compared with volume-controlled ventilation. Br J Anaesth 2008; 100: 709–16
- 16 Olimpio MA, Younggblood BL, James RL. Emergence from anesthesia in the prone versus supine position in patients undergoing lumbar surgery. *Anesthesiology* 2000; **93**: 959–63
- 17 Hohlrieder M, Tiefenthaler W, Klaus H, et al. Effect of total intravenous anaesthesia and balanced anaesthesia on the frequency of coughing during emergence from the anaesthesia. Br J Anaesth 2007; **99**: 587–91
- 18 Joris J, Kaba A. Postoperative spirometry after laparoscopy for lower abdominal or upper abdominal surgical procedures. Br J Anaesth 1997; 79: 422–6
- 19 Hedenstierna G, Tokics L, Lundquist H, et al. Phrenic nerve stimulation during halothane anesthesia. Effects of atelectasis. Anesthesiology 1994; 80: 751–60
- 20 Langeron O, Bouhemad B, Orliaguet G, Coriat P, Lecarpentier Y, Riou B. Effects of halogenated anaesthetics on diaphragmatic actin-myosin cross-bridge kinetics. Br J Anaesth 2003; 90: 759–65
- 21 Ide T, Kochi T, Isono S, Mizuguchi T. Effect of sevoflurane on diaphragmatic contractility in dogs. *Anesth Analg* 1992; **74**: 739–46
- 22 Zhang XJ, Yu G, Wen XH, *et al.* Effect of propofol on twitch diaphragmatic pressure evoked by cervical magnetic stimulation in patients. *Br J Anaesth* 2009; **102**: 61–4
- 23 Jensen AG, Kalman SH, Eintrei C, Fransson SG, Morales O. Atelectasis and oxygenation in major surgery with either propofol with

or without nitrous oxide or isoflurane anaesthesia. *Anaesthesia* 1993; **48**: 1094–6

- 24 Magnusson L, Tenling A, Lemoine R, Högman M, Tydén H, Hedenstierna G. The safety of one, or repeated, vital capacity maneuvers during general anesthesia. *Anesth Analg* 2000; **91**: 702–7
- 25 Prakash YS, Iyanoye A, Ay B, Sieck GC, Pabelick CM. Store-operated Ca<sup>2+</sup> influx in airway smooth muscle: interactions between volatile anesthetic and cyclic nucleotide effects. *Anesthesiology* 2006; **105**: 976–83
- 26 von Ungern-Sternberg BS, Regli A, Reber A, Schneider MC. Effect of obesity and thoracic epidural analgesia on perioperative spirometry. Br J Anaesth 2005; 94: 121–7

- 27 Wahba WM, Don HF, Craig DB. Post-operative epidural analgesia: effects on lung volumes. *Can Anaesth Soc J* 1975; **22**: 519–27
- 28 Gunaydin B, Ozulgen IK, Ozturk E, Tekgul ZT, Kaya K. Remifentanil versus remifentanil with paracervical block on plasma remifentanil concentrations and pulmonary function tests for transvaginal ultrasound-guided oocyte retrieval. J Opioid Manag 2007; 3: 267–72
- 29 De Baerdemaeker LE, Jacobs S, Pattyn P, Mortier EP, Struys MM. Influence of intraoperative opioid on postoperative pain and pulmonary function after laparoscopic gastric banding: remifentanil TCI vs sufentanil TCI in morbid obesity. Br J Anaesth 2007; 99: 404-11