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Development of atelectasis and arterial to end-tidal P_{CO_2}-difference in a porcine model of pneumoperitoneum

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Background. Intraperitoneal insufflation of carbon dioxide (CO_2) may promote collapse of dependent lung regions. The present study was undertaken to study the effects of CO_2-pneumoperitoneum (CO_2-PP) on atelectasis formation, arterial oxygenation, and arterial to end-tidal P_{CO_2}-gradient ($Pa\text{-}E'_{CO_2}$).

Methods. Fifteen anaesthetized pigs [mean body weight 28 (SD 2) kg] were studied. Spiral computed tomography (CT) scans were obtained for analysis of lung tissue density. In Group 1 (n=5) mechanical ventilation (V_T=10 ml kg $^{-1}$, $F_{I_{O_2}}$=0.5) was applied, in Group 2 (n=5) $F_{I_{O_2}}$ was increased for 30 min to 1.0 and in Group 3 (n=5) negative airway pressure was applied for 20 s in order to enhance development of atelectasis. Cardiopulmonary and CT data were obtained before, 10, and 90 min after induction of CO_2-PP at an abdominal pressure of 12 mmHg.

Results. Before CO_2-PP, in Group 1 non-aerated tissue on CT scans was 1 (1)%, in Group 2 3 (2)% ($P<0.05$, compared with Group 1), and in Group 3 7 (3)% ($P<0.05$, compared with Group 1 and Group 2). CO_2-PP significantly increased atelectasis in all groups. $Pa_{O_2}/F_{I_{O_2}}$ fell and venous admixture ('shunt') increased in proportion to atelectasis during anaesthesia but CO_2-PP had a varying effect on $Pa_{O_2}/F_{I_{O_2}}$ and shunt. Thus, no correlation was seen between atelectasis and $Pa_{O_2}/F_{I_{O_2}}$ or shunt when all data before and during CO_2-PP were pooled. $Pa\text{-}E'_{CO_2}$, on the other hand correlated strongly with the amount of atelectasis (r^2=0.92).

Conclusions. Development of atelectasis during anaesthesia and PP may be estimated by an increased $Pa\text{-}E'_{CO_2}$.

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Intraperitoneal insufflation of carbon dioxide (CO_2) is commonly used for induction of pneumoperitoneum (PP) during laparoscopic surgery.[1] An increased intra-abdominal pressure may shift the end-expiratory position of the diaphragm, decrease functional residual capacity, and induce collapse of dependent lung regions, and even more so in patients with morbid obesity.[2 3] Perfusion of non-ventilated alveoli strongly affects oxygenation of blood[4] and CO_2-elimination may also be impaired. In anaesthetized patients, PP causes an increase in atelectasis but need not increase shunt or lower arterial oxygenation.[5 6] This apparent paradox has not yet been explained. Another consequence of the absence of a correlation between atelectasis and oxygenation is that measurement of Pa_{O_2} or calculation of shunt cannot be used to assess the amount of collapsed lung. The present study was undertaken to study the effects of CO_2-PP on atelectasis formation and arterial to end-tidal P_{CO_2}-gradient ($Pa\text{-}E'_{CO_2}$). We hypothesized that there was a correlation between regional lung collapse and CO_2-elimination in a porcine model of PP.

Methods

After approval by the local animal ethics committee, 15 2-month-old healthy piglets [mean body weight 28 (2) kg,

eight males and seven females) of the Hampshire, Yorkshire, and Swedish country breeds from a local breeder were studied.

Anaesthesia and mechanical ventilation

All pigs were anaesthetized by an i.m. injection of xylazine (2.2 mg kg^{-1}, Rompun®; Bayer, Leverkusen, Germany), tiletamine/zolazepam (6 mg kg^{-1}, Zoletil®; Virbac, Carros, France), and atropine (0.04 mg kg^{-1}, NM Pharma, Stockholm, Sweden). The pigs' lungs were mechanically ventilated after intubation with an ID 7.0 mm cuffed tracheal tube (Mallinckrodt, Athlone, Ireland). Anaesthesia was maintained by continuous administration of fentanyl (5 μg kg^{-1} h^{-1}, Leptanal®; Janssen-Cilag AB, Sweden), pancuronium (0.3 mg kg^{-1} h^{-1}, Pavulon®; Organon, Oss, The Netherlands), ketamine (25 mg kg^{-1} h^{-1}, Ketaminol vet.®; Intervet, Boxmeer, The Netherlands), and propofol (3 mg kg^{-1} h^{-1}, Diprivan®; Astra, Södertälje, Sweden). Before experimentation, adequate depth of surgical anaesthesia was confirmed by absence of both the hind limb flexion reflex and corneal reflex responses according to the laboratory standard of the Animal Ethics Committee of Uppsala University. Ringer's acetate (Pharmacia AB; Stockholm, Sweden) was infused with an average rate of 5 ml kg^{-1} h^{-1} to maintain a constant haemoglobin concentration and stable systemic arterial blood pressure.

Mechanical ventilation was initiated in volume-controlled mode [intermittent positive pressure ventilation (IPPV); Servo i; Maquet Critical Care AB, Solna, Sweden]. Ventilatory frequency was adjusted to achieve normocapnia (Pa_{CO_2}=4.7–6 kPa). Tidal volume (V_t), airway pressures (P_{aw}), and flow were continuously recorded. Static compliance (C_{rs}) of the total respiratory system was calculated as $C_{rs}=V_t\ (P_{aw\ plateau} - P_{aw\ end\text{-}expiration})$.

Monitoring

For pressure measurements and arterial blood sampling, an 18-gauge catheter (Hydrocath™; Becton Dickinson, Franklin Lakes, NJ, USA) was inserted into the left carotid artery. A thermistor-tipped Swan-Ganz catheter (CritiCath™ SP5107H-14 TD; Becton Dickinson) and an 18-gauge catheter (Hydrocath™; Becton Dickinson) were introduced into the left external jugular vein. Systemic, pulmonary arterial, and central venous pressures were displayed on a monitor (SC 9000 XL; Maquet Critical Care AB, Solna, Sweden) and were recorded with reference to atmospheric pressure at the midthoracic level during end-expiration. End-expiratory CO_2 tension ($P_{E'_{CO_2}}$) was measured by capnography implemented in the ventilator (Servo i; Maquet Critical Care AB, Solna, Sweden).

Arterial and mixed venous blood samples were analysed with ABL 300 blood gas analyser and OSM 3 oximeter (Radiometer, Copenhagen, Denmark). Cardiac output (CO) was determined by thermodilution. The thermal indicator was 10 ml of saline 8–10°C and was injected into the right atrium. The first measurement was ignored and the cardiac output was derived from the mean of three consecutive measurements. The injections were evenly distributed over the respiratory cycle. Venous admixture ('shunt') was calculated according to the standard shunt equation, based on the calculation of oxygen content in arterial, mixed venous, and pulmonary end-capillary blood.

Computed tomography

A frontal tomogram of the chest was obtained during ventilation to determine the borders of the lung. An end-expiratory transversal spiral computed tomography (CT; 140 kV, 111 mA) covering the whole lung, with 1 mm slice thickness was acquired with a Somatom Plus 4 CT scanner (Siemens, Erlangen, Germany). The scanning time for the transverse images was approximately 3 s. The CT scanning was analysed using the custom-made software package MALUNA (Mannheim Lung Analysis Tool). The total lung volume was calculated by creating a region of interest (ROI) around each lung scan excluding the mediastinum and the big vessels. Each voxel of the CT scan is characterized by a CT number, which is related to the tissue density and numerically expressed in Hounsfield units (HU). The scale ranges from +1000 HU (bone) to 0 HU (water) and −1000 HU (air). For example, a voxel with −200 HU consists of 20% gas and 80% tissue, and a voxel with −700 HU consists of 70% gas and 30% tissue. For further analysis, the lung was divided into four categories: areas with densities ranging from −1000 to −850 HU were classified as over-aerated, from −850 to −500 HU as normally aerated, from −500 to −100 HU as poorly aerated, and from −100 to +100 HU as non-aerated (atelectasis).

Study protocol

Allocation to the groups was made using sealed envelopes. In Group 1 (n=5), pigs were ventilated with a V_T of 10 ml kg^{-1}, $F_{I_{O_2}}$ of 0.5 and PEEP of 5 cm H_2O. Based on data from the literature and results from our laboratory minor development of atelectasis was expected. In Group 2 (n=5), $F_{I_{O_2}}$ was increased to 1.0 for 30 min and in Group 3 (n=5) a negative pressure of −15 cm H_2O was applied to the tracheal tube for 20 s in order to produce a large range of atelectasis similar to findings in anaesthetized normal-weight and morbidly obese patients. After these procedures, Group 2 and Group 3 were given the same ventilation as Group 1.

Pneumoperitoneum was created by insufflation of CO_2 into the abdominal cavity via a VERRES needle with a common CO_2 insufflator (7060-Insufflator Pelvi Pneu Semm Systems; Wisap, Munich, Germany) until the abdominal pressure (P_{abd}) reached 12 mmHg. Mechanical

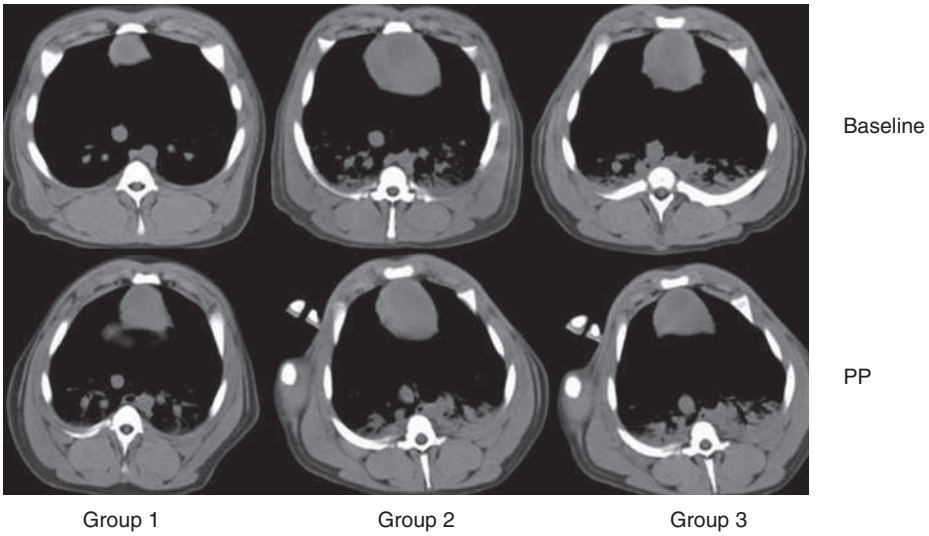

Fig 1 Example of computed tomography (CT) scans during anaesthesia (baseline) and during CO_2-pneumoperitoneum in all groups.

ventilation was maintained in the same mode and pattern as before induction of PP. Measurements of gas exchange and haemodynamics and recordings with CT were made during anaesthesia after the period of $F_{I_{O_2}}$ 1.0 in Group 2 and negative pressure in Group 3, before and after 10 and 90 min of CO_2-PP.

After completion of the experiment, the pigs were killed by an i.v. bolus injection of potassium chloride (150 mval).

Statistics

Statistical analysis was performed with the JNP IN 5.1 software package (SAS Institute Inc., Cary, NC, USA) on a Macintosh computer. Power calculations using a two-sided design at a significance level of 5% (a=0.05) and a probability of 80% (b=0.20) to detect a difference of at least 35% in the development of atelectasis revealed that a minimum of five pigs was needed in each group.

Data were tested for normal distribution with the Shapiro-Wilks W test. Normally distributed data are presented as mean (SD) (cardiopulmonary, ventilation, and gas exchange variables). These data were analysed by a repeated measures one-way ANOVA with *post hoc* Bonferroni correction. Non-normally distributed data were analysed by Friedman's ANOVA and Tukey's HSD. Comparison between two variables was tested by linear regression analysis. CT data were slice-wise analysed by two-sample t-tests and repeated measures ANOVA. Differences were considered to be statistically significant for all procedures if $P<0.05$.

Results

Examples of CT scans after induction of anaesthesia and during CO_2-PP are shown in Figure 1. In Group 1 little atelectasis was detected by CT. Oxygenation was normal [$Pa_{O_2}/F_{I_{O_2}}$=62 (3.7) kPa] and shunt was small [2.8 (0.5)%] and $Pa\text{-}E'_{CO_2}$ was low [0.04 (0.05) kPa]. In Group 2 atelectasis had increased to 3 (2)% ($P<0.05$ compared with Group 1). Oxygenation was slightly impaired [$Pa_{O_2}/F_{I_{O_2}}$=50 (8) kPa], shunt had risen to 10.9 (3.4)% ($P<0.05$ compared with Group 1) and $Pa\text{-}E'_{CO_2}$ had increased to 0.3 (0.07) kPa. In Group 3 atelectasis had increased to 7 (3)% ($P<0.05$ compared with Group 1 and Group 2). Likewise, $Pa_{O_2}/F_{I_{O_2}}$ [34 (8.4) kPa, $P<0.05$], shunt [14.2 (3)%, $P<0.05$], and $Pa\text{-}E'_{CO_2}$ [0.6 (0.2) kPa, $P<0.05$] were significantly different when compared with Group 1 and Group 2 (Table 1).

Induction of CO_2-PP increased atelectasis and $Pa\text{-}E'_{CO_2}$ in all groups (although not significantly for atelectasis in Group 1) (Table 1). There was a significant correlation between the amount of atelectasis and $Pa\text{-}E'_{CO_2}$ in each group before and during CO_2-PP and when all data were pooled (r^2=0.92; Fig. 2). There was good correlation between oxygenation and the amount of atelectasis before (r^2=0.91), but not after induction of CO_2-PP (r^2=0.36; Fig. 3). Correlation between shunt and amount of atelectasis was even poorer than between oxygenation and amount of atelectasis (r^2=0.26).

During PP mean airway pressure and mean pulmonary arterial pressure increased significantly, whereas cardiac output and mean arterial pressure remained unchanged. C_{rs} was significantly lower during CO_2-PP (Table 1). Normally aerated lung was decreased approximately in inverse proportion to the increase of atelectasis formation during intraperitoneal CO_2-insufflation (Table 1). There were no differences between 10 min and 90 min of CO_2-PP (data shown in figures have been taken from the 90-min recordings).

Discussion

The main findings of the present study are that the atelectasis that developed during anaesthesia in a porcine model

Table 1 Measurements from the spiral computed tomography and ventilatory and circulatory variables. Baseline=measurement before insufflation of CO_2-pneumoperitoneum (CO_2-PP); 10 min PP=10 min after insufflation of CO_2-PP, 90 min PP=90 min after insufflation of CO_2-PP; Group 1=FI_{O_2} 0.5; V_T of 10 ml kg^{-1} and PEEP 5 cm H_2O; Group 2=FI_{O_2} temporarily increased to 1.0; Group 3=a negative pressure of −15 mm H_2O was applied to the tracheal tube for 20 s; atelectasis=−100 to 100 HU; poor aeration=−500 to −100 HU; normal aeration=−850 to −500 HU; over aeration=−850 to −1000 HU; FI_{O_2}/Pa_{O_2}=ratio of inspiratory fraction of oxygen and arterial oxygen tension; cQ_S/Q_T=calculated intrapulmonary shunt; Pa_{CO_2}=arterial carbon dioxide tension; PE'_{CO_2}=end-expiratory carbon dioxide tension; $Pa\text{-}E'_{CO_2}$=difference between arterial and end-expiratory PCO_2; P_{aw} peak=peak airway pressure; C_{rs}=respiratory compliance. Data are given as mean (SD; n=5); *P-value ($P<0.05$) in comparison with baseline measurements

Variable	Baseline (before PP)			10 min PP			90 min PP		
	Group 1 (n=5)	Group 2 (n=5)	Group 3 (n=5)	Group 1 (n=5)	Group 2 (n=5)	Group 3 (n=5)	Group 1 (n=5)	Group 2 (n=5)	Group 3 (n=5)
Atelectasis (%)	1 (1)	3 (2)	7 (3)	3 (2)	7 (2)*	13 (1)*	3 (3)	9 (2)**	13 (3)*
Poor aeration (%)	45 (9)	43 (8)	42 (8)	50 (10)	46 (6)	50 (13)	43 (7)	49 (6)	52 (11)
Normal aeration (%)	53 (10)	52 (7)	51 (9)	46 (11)	45 (5)*	38 (13)*	51 (9)	41 (6)**	36 (12)*
Over aeration (%)	0.8 (0.9)	0.7 (0.4)	0.13 (0.17)	0.6 (0.4)	0.5 (0.3)	0.16 (0.23)	0.7 (0.9)	0.5 (0.2)	0.11 (0.13)
Pa_{O_2}/FI_{O_2} (kPa)	62 (3.7)	50 (8)	34 (8.4)	59 (8.1)	34 (11)*	41 (4.3)	56 (8.2)	41 (5.7)*	46 (2.4)*
Shunt (%)	2.8 (0.5)	10.9 (3.4)	14.2 (3)	2.6 (1)	13.6 (3)*	12.7 (3.2)	2.9 (1.1)	11.7 (1.7)	10.5 (1)*
Pa_{CO_2} (kPa)	5.2 (0.4)	5.6 (0.5)	5.2 (0.5)	6.5 (0.5)*	6.5 (0.3)*	6.3 (0.3)*	7 (0.7)*	6.7 (0.4)*	6.5 (0.3)*
PE'_{CO_2} (kPa)	5.2 (0.3)	5.5 (0.3)	4.7 (0.3)	5.9 (0.4)*	5.7 (0.4)	5.5 (0.3)*	6.5 (0.7)*	6 (0.4)	5.7 (0.1)*
$Pa\text{-}E'_{CO_2}$ (kPa)	0.04 (0.05)	0.1 (0.05)	0.6 (0.2)	0.3 (0.1)*	0.6 (0.07)*	0.8 (0.2)*	0.3 (0.08)*	0.7 (0.05)*	0.8 (0.2)*
P_{aw} peak (cm H_2O)	21 (1)	24 (3)	21 (2)	30 (2)*	31 (4)*	29 (2)*	32 (3)*	32 (5)*	31 (3)*
C_{rs} (ml cm^{-1} H_2O)	20 (3)	16 (2)	16 (2)	12 (2)*	11 (1)*	10 (0.5)*	11 (2)*	11 (1)*	9 (0.5)*

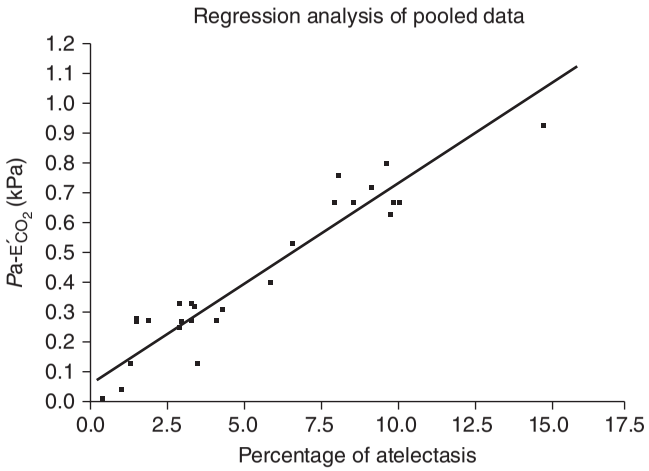

Fig 2 Plot of $Pa\text{-}E'_{CO_2}$ *vs* atelectasis in all groups. The linear regression analysis resulted in the equation $Y=0.06X+0.66$, $r^2=0.92$. A good correlation was seen when all data were pooled. Separate regression equations for data obtained during anaesthesia before and during CO_2-pneumoperitoneum, respectively, did not differ from the overall regression and are not shown.

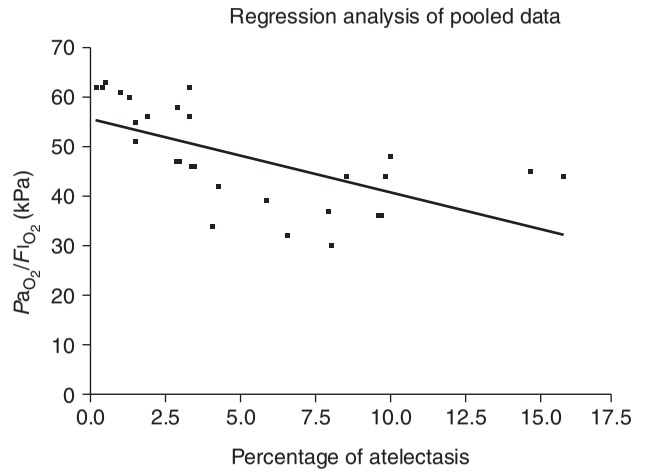

Fig 3 Plot of Pa_{O_2}/FI_{O_2} *vs* atelectasis in all groups. The linear regression analysis resulted in the equation $Y=55.6X-1.47$, $r^2=0.40$. No significant correlation was seen during CO_2-PP when all data were pooled. Separate regression analysis of Pa_{O_2}/FI_{O_2} *vs* atelectasis during CO_2-PP showed even poorer correlation ($r^2=0.36$).

increased further during CO_2-PP with no worsening of Pa_{O_2}/FI_{O_2} but with an increase in $Pa\text{-}E'_{CO_2}$. Thus, Pa_{O_2}/FI_{O_2} did not correlate with atelectasis during PP, precluding arterial oxygenation as a predictor of the amount of collapsed lung. On the other hand, the strong correlation between $Pa\text{-}E'_{CO_2}$ and the amount of atelectasis makes $Pa\text{-}E'_{CO_2}$ of potential value in predicting atelectasis during anaesthesia and CO_2-PP.

Intraperitoneal insufflation of CO_2 has different effects on the respiratory system. In supine human subjects, CO_2-PP at an abdominal pressure of 12 mmHg caused a cranial shift of the diaphragm of 1–3 cm, decreased lung volumes, and increased airway pressures.[3 7] Clinical

studies have also demonstrated development of atelectasis in dependent lung regions after induction of anaesthesia.[8 9] The magnitude of atelectasis in the present study corresponds to findings in non-obese patients (Group 1 and Group 2) and obese patients with a body mass index >30 kg m^{-2} (Group 3).[2 10 11]

The aggravation of atelectasis caused by induction of CO_2-PP was not paralleled by increased shunt or impaired arterial oxygenation. Thus, an increased atelectasis but a decreased intrapulmonary shunt (Qs/Qt) and increased Pa_{O_2} were demonstrated in supine patients 45 min after intraperitoneal CO_2-insufflation.[5] Consequently, oxygenation indices may not adequately reflect the magnitude of lung collapse during PP.

$Pa\text{-}E'_{CO_2}$ can be increased either by an increase in Pa_{CO_2} or a decrease in PE'_{CO_2}. The former occurs when mixed venous blood passes through the lung through shunt vessels without delivering CO_2 to alveolar air, as in atelectatic tissue. The latter occurs when there is a parallel dead space, as ventilation of non-perfused or poorly perfused alveoli, that is $V_D$alv.[12–14]

When shunt is small the effects on $Pa\text{-}E'_{CO_2}$ are negligible, but large shunts can increase $Pa\text{-}E'_{CO_2}$.[13] This phenomenon has been termed 'shunt dead space' although it has nothing to do with dead space.[15] The magnitude of shunt was moderate in the present study but enough to cause a modest increase in $Pa\text{-}E'_{CO_2}$, as deducted from mathematical modelling.[12 13] Moreover, when ventilated lung is reduced by the cranial displacement of the diaphragm during CO_2-PP (with subsequent increase in atelectasis formation), a shift of ventilation can be anticipated so that previously normally ventilated regions become over-ventilated in relation to their perfusion. If an alveolar dead space is calculated by standard formula on CO_2 elimination $[(Pa_{CO_2}-PE'_{CO_2})/Pa_{CO_2}]$, then a linear correlation between atelectasis and $V_D$alv was found (r^2=0,68) with an, on average, 12% increase during CO_2-PP. This fits with a redistribution of ventilation with excessive ventilation of previously more normally ventilated regions, keeping in mind the limited ability by the CO_2 technique to discriminate between 'true' $V_D$alv and high ventilation in relation to perfusion. We have refrained from making this an original observation in the Results section because of the similarity between the equation for $V_D$alv and the expression $Pa\text{-}E'_{CO_2}$. Moreover, the correlation is less good for $V_D$alv than for $Pa\text{-}E'_{CO_2}$ (r^2=0.92), suggesting that $V_D$alv and shunt act in common to produce the elevated $Pa\text{-}E'_{CO_2}$.

Limitations of the study include the small number of animals and that conditions of lung disease have not been studied. In addition, hypoxic pulmonary vasoconstriction is more developed in pigs than in humans.[16 17] Hypoxic vasoconstriction will decrease blood flow to the non-ventilated lung and consequently $Pa\text{-}E'_{CO_2}$. Ventilation pattern was not changed during the study, which induced mild hypercapnia during CO_2-PP in all animals. In a clinical setting minute ventilation might be increased during intraperitoneal CO_2-insufflation in order to maintain normocarbia, which may affect $Pa\text{-}E'_{CO_2}$. However, the magnitude of Pa_{CO_2} should have no effect on the $Pa\text{-}E'_{CO_2}$.[12]

In conclusion we have shown a significant correlation between the magnitude of atelectasis and $Pa\text{-}E'_{CO_2}$ in a porcine model of PP. Thus, assessment of $Pa\text{-}E'_{CO_2}$ may help to quantify the amount of atelectasis in patients undergoing laparoscopic surgery. However, this has to be validated under clinical conditions. Moreover, whether this relationship can be demonstrated in the presence of lung disease also remains to be shown.

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References

1 Neudecker J, Sauerland S, Neugebauer E, *et al*. The European Association for Endoscopic Surgery clinical practice guideline on the pneumoperitoneum for laparoscopic surgery. *Surg Endosc* 2002; **16**: 1121–43

2 Nguyen NT, Wolfe BM. The physiologic effects of pneumoperitoneum in the morbidly obese. *Ann Surg* 2005; **241**: 219–26

3 El-Dawlatly AA, Al-Dohayan A, Abdel-Meguid ME, El-Bakry A, Manaa EM. The effects of pneumoperitoneum on respiratory mechanics during general anesthesia for bariatric surgery. *Obes Surg* 2004; **14**: 212–5

4 Duggan M, Kavanagh BP. Atelectasis in the perioperative patient. *Curr Opin Anaesthesiol* 2007; **20**: 37–42

5 Andersson L, Lagerstrand L, Thorne A, Sollevi A, Brodin LA, Odeberg-Wernerman S. Effect of CO(2) pneumoperitoneum on ventilation-perfusion relationships during laparoscopic cholecystectomy. *Acta Anaesthesiol Scand* 2002; **46**: 552–60

6 Meininger D, Zwissler B, Byhahn C, Probst M, Westphal K, Bremerich DH. Impact of overweight and pneumoperitoneum on hemodynamics and oxygenation during prolonged laparoscopic surgery. *World J Surg* 2006; **30**: 520–6

7 Andersson LE, Baath M, Thorne A, Aspelin P, Odeberg-Wernerman S. Effect of carbon dioxide pneumoperitoneum on development of atelectasis during anesthesia, examined by spiral computed tomography. *Anesthesiology* 2005; **102**: 293–9

8 Rothen HU, Sporre B, Engberg G, Wegenius G, Hedenstierna G. Re-expansion of atelectasis during general anaesthesia: a computed tomography study. *Br J Anaesth* 1993; **71**: 788–95

9 Coussa M, Proietti S, Schnyder P, *et al*. Prevention of atelectasis formation during the induction of general anesthesia in morbidly obese patients. *Anesth Analg* 2004; **98**: 1491–5 table of contents

10 McAlister FA, Bertsch K, Man J, Bradley J, Jacka M. Incidence of and risk factors for pulmonary complications after nonthoracic surgery. *Am J Respir Crit Care Med* 2005; **171**: 514–7

11 Hedenstierna G, Rothen HU. Atelectasis formation during anesthesia: causes and measures to prevent it. *J Clin Monit Comput* 2000; **16**: 329–35

12 Hardman JG, Aitkenhead AR. Estimating alveolar dead space from the arterial to end-tidal CO(2) gradient: a modeling analysis. *Anesth Analg* 2003; **97**: 1846–51

13 Fletcher R, Jonson B. Deadspace and the single breath test for carbon dioxide during anaesthesia and artificial ventilation. Effects of tidal volume and frequency of respiration. *Br J Anaesth* 1984; **56**: 109–19

14 Fletcher R. The relationship between the arterial to end-tidal PCO2 difference and hemoglobin saturation in patients with congenital heart disease. *Anesthesiology* 1991; **75**: 210–6

15 Hedenstierna G, Sandhagen B. Assessing dead space. A meaningful variable? *Minerva Anesthesiol* 2006; **72**: 521–8

16 Hedenstierna G, Hammond M, Mathieu-Costello O, Wagner PD. Functional lung unit in the pig. *Respir Physiol* 2000; **120**: 139–49

17 Tucker A, McMurtry IF, Reeves JT, Alexander AF, Will DH, Grover RF. Lung vascular smooth muscle as a determinant of pulmonary hypertension at high altitude. *Am J Physiol* 1975; **228**: 762–7