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# Effects of abdominal CO<sub>2</sub> insufflation and changes of position on hepatic blood flow in anesthetized pigs

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**Klopfenstein, Claude-Eric, Denis R. Morel, François Clergue, and Catherine M. Pastor.** Effects of abdominal CO<sub>2</sub> insufflation and changes of position on hepatic blood flow in anesthetized pigs. *Am. J. Physiol.* 275 (*Heart Circ. Physiol.* 44): H900–H905, 1998.—During surgical laparoscopy, total hepatic blood flow (THBF) may be modified by CO<sub>2</sub> insufflation, changes of tilt, ventilation with high tidal volume, hypercapnia, and anesthesia, but little information is available on the THBF during the procedure. To investigate the changes of hepatic blood flow following the combination of abdominal CO<sub>2</sub> insufflation and changes of tilt, we measured mean arterial pressure (MAP), cardiac output, portal vein blood flow (PVBF), and hepatic artery blood flow (HABF) in anesthetized and ventilated pigs. CO<sub>2</sub> was insufflated in the abdomen [intra-abdominal pressure (IAP) ~15 mmHg], and the hepatic blood flow was measured in various positions (horizontal, 10° and 20° head down, and 10° and 20° head up) before and during CO<sub>2</sub> insufflation. CO<sub>2</sub> insufflation in the horizontal position did not modify MAP, cardiac output, or PVBF but increased HABF. The head-up tilt decreased MAP, cardiac output, and both hepatic flows in the absence of pneumoperitoneum, but in the presence of abdominal CO<sub>2</sub> only cardiac output and PVBF were decreased. The head-down tilt increased MAP and THBF in the absence of pneumoperitoneum, whereas no change was observed in the presence of abdominal CO<sub>2</sub>. The combination of CO<sub>2</sub> insufflation and changes of tilt was not deleterious to hepatic perfusion. These results suggest that hepatic blood flow may be preserved during surgical laparoscopy if the tilt does not exceed 20° and if IAP after CO<sub>2</sub> insufflation remains <15 mmHg.

intra-abdominal pressure; tilt

DURING LAPAROSCOPIC PROCEDURES abdominal organs are visualized by intraperitoneal insufflation of gas (mostly CO<sub>2</sub>). To facilitate access to organs in the upper or lower part of the abdomen, the pneumoperitoneum is combined with head-up or head-down tilts. Despite the hemodynamic and respiratory consequences of increased intra-abdominal pressures (IAP), laparoscopic surgery has been found to offer several advantages such as reduced postoperative pulmonary dysfunction and short hospitalization time (27–29). If for many years, gynecologic laparoscopy was performed mainly in young, healthy patients, this technique is now applied in general surgery for various and long-lasting operations and involves older patients suffering from patent or unknown diseases. Therefore, the consequences of elevated IAP and changes in position may increase the morbidity rate of these patients.

Although ventilatory and hemodynamic changes during surgical laparoscopy have been extensively investigated in humans, little information is available on hepatic blood flow during the procedure. The consequences of IAP increase on hepatic blood flow have already been studied in various experimental models. In anesthetized pigs, Diebel et al. showed that a 20-mmHg increase in IAP (induced by fluid infusion in the abdomen) decreased hepatic (5) as well as mesenteric (4) perfusion. In contrast, in anesthetized dogs, increasing IAP up to 20 mmHg by CO<sub>2</sub> insufflation did not compromise mesenteric blood flow (16). When IAP was increased by inflating a large bag into the peritoneum hepatic artery blood flow (HABF) increased, but this increase was not sufficient to maintain total hepatic blood flow (THBF) (21). The consequences of various positions such as head-down and head-up tilts on hepatic blood flow are also unknown. Moreover, hypercapnia, ventilation with high tidal volume, and anesthetic agents may also interfere with hepatic blood flow during surgical laparoscopy. The aim of the present study was to investigate the modifications of hepatic blood flow after CO<sub>2</sub> insufflation and changes of tilt in anesthetized pigs.

## METHODS

**Animals and anesthesia.** Male or female domestic pigs (21–28 kg,  $n = 9$ ) were fasted with free access to water for 24 h before the experiment, premedicated, and placed in a supine position on the operating table with the front- and hindlimbs fixed in the abduction position. After induction of anesthesia with halothane, pigs were intubated and mechanically ventilated with air and O<sub>2</sub> (fractional inspired O<sub>2</sub> = 0.4) to obtain normal arterial pH and arterial PCO<sub>2</sub> (PaCO<sub>2</sub>) between 36 and 42 mmHg. After intubation, halothane was withdrawn and anesthesia was maintained with thiopental (5 mg·kg<sup>-1</sup>·h<sup>-1</sup>) and fentanyl (10–20 µg·kg<sup>-1</sup>·h<sup>-1</sup>). Pancuronium (0.2 mg·kg<sup>-1</sup>·h<sup>-1</sup>) was used as a skeletal muscle relaxant. The protocol was approved by the Animal Welfare Committee of the University of Geneva and the Veterinary Office and followed the Guidelines for the Care and Use of Laboratory Animals.

**Surgical procedure.** The right carotid artery was cannulated to measure mean arterial pressure (MAP, mmHg) and to collect blood samples. A catheter was inserted into the right external jugular vein to provide fluid and drugs. A pulmonary artery catheter (131H-7F, Baxter, Düringen, Switzerland) was inserted through the right internal jugular vein to measure mean pulmonary arterial pressure (MPAP, mmHg), central venous pressure (CVP, mmHg), pulmonary capillary wedge pressure (PCWP, mmHg), and cardiac output (l/min).

After a midline abdominal incision, the bladder was drained. Two flow probes were positioned around the portal vein and the hepatic artery (upstream from the bifurcation of the common hepatic artery and the gastroduodenal artery) to determine portal vein blood flow (PVBF, ml/min) and HABF (ml/min). Blood flows were measured with the ultrasound transit time technique (Transonic System, Ithaca, NY). To measure portal vein pressure (PVP, mmHg) and hepatic vein pressure (HVP, mmHg), catheters were inserted into the portal vein through a side branch and 1–2 cm into a hepatic vein through the left external jugular vein, respectively. Location of the catheter tips was confirmed by direct palpation. Thereafter, a catheter was positioned in the abdomen and the abdominal wall was tightly closed. All transducers were zeroed to the midchest of the animals. Core temperature was maintained (37–38°) with heating lamps. Animals were infused with 0.9% saline and 2.5% dextrose solutions (12 ml·kg<sup>-1</sup>·h<sup>-1</sup> during surgery and 8 ml·kg<sup>-1</sup>·h<sup>-1</sup> during experimental protocol) to compensate for fluid loss induced by anesthesia and surgery.

**Experimental protocol.** After the animals were anesthetized and instrumented, a 2-h recovery period was observed for the stabilization of hemodynamic and biologic variables. Under stable anesthesia, respiratory and hemodynamic measurements were performed in the horizontal position, with 10 and 20° head-down and 10 and 20° head-up tilts. Variables were allowed to stabilize for 5 min before data collection. Thereafter, to create the pneumoperitoneum, intra-abdominal CO<sub>2</sub> was insufflated through a Verres needle by an automatic insufflator (26012, Storz, Tuttlingen, Germany). CO<sub>2</sub> was insufflated in the horizontal position until IAP reached ~15 mmHg. Measurements were then repeated in the five different positions. Head-down and head-up tilts were randomized, whereas the amplitude of tilt was not. Data were collected in the horizontal position after the recovery period (H1), after head-down and head-up tilts (H2 and H3), after CO<sub>2</sub> insufflation (H4), after head-down and head-up tilts during pneumoperitoneum (H5 and H6), and after CO<sub>2</sub> exsufflation (H7). During the protocol, minute ventilation was adjusted to obtain normal PCO<sub>2</sub> by increasing tidal volume. A tilt of ≤20° and an IAP increase of ≤15 mmHg were chosen because we wanted to mimic the tilt and IAP increase commonly used in clinical laparoscopy.

**Systemic and hepatic oxygenation.** Expired flow from the ventilator was directly connected to a metabolic measurement cart (Datex, Helsinki, Finland) for continuous measurements of O<sub>2</sub> consumption ( $\dot{V}O_2$ , ml/min) and CO<sub>2</sub> production ( $\dot{V}CO_2$ , ml/min). O<sub>2</sub> contents in the carotid artery, the portal vein, and the hepatic vein were determined in blood samples obtained from the appropriate catheters and analyzed for PO<sub>2</sub>, Hb concentration, and fractional O<sub>2</sub> saturation (SO<sub>2</sub>).

O<sub>2</sub> content was calculated according to the equation

$$O_2 \text{ content} = (PO_2 \cdot 0.003) + (Hb \cdot SO_2 \cdot 1.36)$$

The following equations were used

$$\text{systDO}_2 = \text{cardiac output} \cdot aO_2 \text{ content}$$

$$\text{haDO}_2 = \text{HABF} \cdot aO_2 \text{ content}$$

$$\text{pvDO}_2 = \text{PVBF} \cdot \text{pvO}_2 \text{ content}$$

$$\text{thDO}_2 = \text{pvDO}_2 + \text{haDO}_2$$

$$\text{hep}\dot{V}O_2 = [(aO_2 \text{ content} \cdot \text{HABF}) + (\text{pvO}_2 \text{ content} \cdot \text{PVBF})] \\ - [\text{hvO}_2 \text{ content} \cdot (\text{HABF} + \text{PVBF})]$$

where the prefixes a, syst, ha, pv, th, and hep are arterial, systemic, hepatic artery, portal vein, total hepatic, and hepatic, respectively, and DO<sub>2</sub> is O<sub>2</sub> delivery.

Lactate uptake (Lac) through the liver was calculated as

$$[(\text{pvLac} \cdot \text{PVBF}) + (\text{haLac} \cdot \text{HABF})] \\ - [\text{hvLac} \cdot (\text{HABF} + \text{PVBF})]$$

**Statistical analysis.** All results were expressed as means ± SE. Data were analyzed using repeated-measures analysis of variance followed by a Scheffé's test to compare mean values. *P* < 0.05 was considered significant.

## RESULTS

**CO<sub>2</sub> variables.** CO<sub>2</sub> variables are given in Table 1. Minute ventilation was adjusted to obtain normal blood gases during CO<sub>2</sub> insufflation as described in METHODS, and consequently Pa<sub>CO<sub>2</sub></sub> and end-tidal CO<sub>2</sub> pressure (PET<sub>CO<sub>2</sub></sub>) did not change during the experimental protocol. Pa<sub>CO<sub>2</sub></sub> – PET<sub>CO<sub>2</sub></sub> remained steady before CO<sub>2</sub> insufflation in the different positions and when CO<sub>2</sub> was insufflated in the horizontal position. However, the combination of head-up 20° tilt and CO<sub>2</sub> insufflation increased Pa<sub>CO<sub>2</sub></sub> – PET<sub>CO<sub>2</sub></sub>. As a consequence of intra-peritoneal CO<sub>2</sub> insufflation,  $\dot{V}CO_2$  significantly increased.

**Hemodynamic variables.** Before CO<sub>2</sub> insufflation, the preparation remained steady because hemodynamic variables were similar in the three control horizontal positions, H1, H2, and H3 (Table 2). After a 20° head-down tilt, MAP, CVP, and MPAP increased, whereas heart rate and PCWP did not change. PVP increased, but HVP did not. Cardiac output and HABF did not change, but PVBF significantly increased (+16%). In the 20° head-up tilt, MAP, MPAP, CVP, PCWP, PVP, and HVP decreased significantly as well as cardiac output

Table 1. CO<sub>2</sub> variables before and during pneumoperitoneum

	Pneumoperitoneum						
	Horizontal H1	Head Down 20°	Head Up 20°	Horizontal H4	Head-down 20°	Head-up 20°	Horizontal H6
Pa <sub>CO<sub>2</sub></sub> , mmHg	37 ± 1	37 ± 1	37 ± 1	40 ± 1	40 ± 1	41 ± 1	40 ± 2
PET <sub>CO<sub>2</sub></sub> , mmHg	35 ± 1	36 ± 1	35 ± 1	37 ± 1	36 ± 1	36 ± 1	36 ± 1
Pa <sub>CO<sub>2</sub></sub> – PET <sub>CO<sub>2</sub></sub> , mmHg	2.2 ± 0.3	1.6 ± 0.4	2.0 ± 0.5	2.9 ± 0.5	3.9 ± 0.5	5.0 ± 0.8*	4.4 ± 1.3
$\dot{V}CO_2$ , ml/min	121 ± 5	121 ± 5	120 ± 7	162 ± 6*	165 ± 6*	158 ± 5*	161 ± 5*

Values are means ± SE. H1, horizontal position without pneumoperitoneum, H4 and H6, horizontal position during pneumoperitoneum. \**P* < 0.05 vs. same position without pneumoperitoneum. Pa<sub>CO<sub>2</sub></sub> and PET<sub>CO<sub>2</sub></sub>, arterial and end-tidal PCO<sub>2</sub>, respectively;  $\dot{V}CO_2$ , CO<sub>2</sub> production.

Table 2. Hemodynamic variables in absence of pneumoperitoneum: effect of horizontal position and head-down and head-up tilts

	Horizontal H1	Head Down 10°	Head Down 20°	Horizontal H2	Head Up 10°	Head Up 20°	Horizontal H3
Heart rate, beats/min	84 ± 3	83 ± 3	85 ± 3	82 ± 3	80 ± 3	81 ± 4	84 ± 4
MAP, mmHg	106 ± 4	112 ± 4	115 ± 4*	104 ± 5	99 ± 5	95 ± 5†	104 ± 4
MPAP, mmHg	19 ± 1	20 ± 1	22 ± 1*	18 ± 1	16 ± 1	15 ± 1†	19 ± 1
CVP, mmHg	7 ± 1	8 ± 1	9 ± 1*	7 ± 1	6 ± 1	5 ± 1†	7 ± 1
PCWP, mmHg	8 ± 1	9 ± 1	9 ± 1	8 ± 1	6 ± 1	5 ± 1†	7 ± 1
PVP, mmHg	10 ± 1	12 ± 1	13 ± 1*	10 ± 1	9 ± 1	7 ± 1†	10 ± 1
HVP, mmHg	9 ± 1	9 ± 1	11 ± 1	8 ± 1	7 ± 1	6 ± 1†	8 ± 1
PVP – HVP, mmHg	2.2 ± 0.5	2.5 ± 0.5	2.3 ± 0.4	2.4 ± 0.6	2.3 ± 0.7	2.0 ± 0.6	2.2 ± 0.6
IAP, mmHg	5.4 ± 0.4	7.3 ± 0.5	9.0 ± 0.6*	5.8 ± 0.5	3.8 ± 0.6	2.5 ± 0.6†	5.4 ± 0.6
CO, l/min	2.3 ± 0.1	2.5 ± 0.1	2.6 ± 0.2	2.4 ± 0.1	2.1 ± 0.1	2.0 ± 0.1†	2.3 ± 0.2
HABF, ml/min	158 ± 29	176 ± 33	187 ± 34	157 ± 28	139 ± 25	125 ± 22†	157 ± 27
PVBF, ml/min	698 ± 34	762 ± 38	806 ± 47*	708 ± 29	656 ± 23	618 ± 25†	734 ± 30
THBF, ml/min	856 ± 41	939 ± 45*	993 ± 53*	865 ± 39	796 ± 32	743 ± 29†	891 ± 41

Values are means ± SE. H2, horizontal after head-down tilt; H3, horizontal after head-up tilt; MAP, mean arterial pressure; MPAP, mean pulmonary arterial pressure; CVP, central venous pressure; PCWP, pulmonary capillary wedge pressure; PVP, portal venous pressure; HVP, hepatic venous pressure; IAP, intra-abdominal pressure; CO, cardiac output; HABF, hepatic artery blood flow; PVBF, portal vein blood flow; THBF, total hepatic blood flow. \*  $P < 0.05$  vs. H1, †  $P < 0.05$  vs. H2.

(–14%), HABF (–19%), and PVBF (–13%). Thus head-down tilt increased THBF, whereas head-up tilt decreased it. The 10° head-up and head-down tilts induced minor modifications.

CO<sub>2</sub> insufflation in the horizontal position (H4 vs. H3 in Table 3 and Fig. 1) increased heart rate, MPAP, CVP, PVP, and HVP, whereas MAP did not change significantly. Cardiac output and PVBF were not modified, but HABF increased (+49%). Despite the significant increase in HABF, because PVBF was not modified, THBF did not change significantly. Opposite effects were observed after CO<sub>2</sub> exsufflation (H7 vs. H6 in Table 3).

During the insufflation (Table 3), the head-down tilt did not change the hemodynamic variables, whereas the 20° head-up tilt decreased PCWP, cardiac output (–18%), and PVBF (–16%). The combination of CO<sub>2</sub> insufflation and 20° head-down tilt increased THBF

(+28%, Fig. 1), whereas the combination of CO<sub>2</sub> insufflation and 20° head-up tilt had no consequence on THBF (–2.3%, Fig. 1).

*Variables of oxygenation.* Variables of oxygenation are given in Table 4. Systemic DO<sub>2</sub> and V̇O<sub>2</sub> significantly changed during the protocol ( $P < 0.001$ ), but no difference was observed when the effects of tilt and CO<sub>2</sub> insufflation were compared. Similar results were found for the hepatic variables of oxygenation. Moreover, CO<sub>2</sub> insufflation and position had no effect on lactate uptake through the liver, and no switch from lactate uptake to lactate release was observed.

**DISCUSSION**

This study clearly shows that THBF increases when anesthetized pigs are positioned in the head-down tilt but decreases when they are in the head-up tilt. CO<sub>2</sub>

Table 3. Hemodynamic variables during pneumoperitoneum: effect of horizontal position and head-down and head-up tilts

	Pneumoperitoneum								
	Horizontal H3	Horizontal H4	Head down 10°	Head down 20°	Horizontal H5	Head up 10°	Head up 20°	Horizontal H6	Horizontal H7
Heart rate, beats/min	84 ± 4	91 ± 4*	91 ± 5	92 ± 5	92 ± 4	90 ± 5	91 ± 5	92 ± 5	92 ± 6
MAP, mmHg	104 ± 4	111 ± 5	110 ± 4	113 ± 4	110 ± 5	106 ± 5	102 ± 5	100 ± 4	93 ± 4
MPAP, mmHg	19 ± 1	24 ± 1*	26 ± 1	27 ± 1	25 ± 1	23 ± 1	23 ± 1	25 ± 2	19 ± 1†
CVP, mmHg	7 ± 1	9 ± 1*	10 ± 1	10 ± 1	9 ± 1	8 ± 1	7 ± 1	8 ± 1	6 ± 1†
PCWP, mmHg	7 ± 1	9 ± 1	11 ± 1	11 ± 1	9 ± 1	8 ± 1	7 ± 1‡	8 ± 1	6 ± 1†
PVP, mmHg	10 ± 1	18 ± 1*	19 ± 1	19 ± 1	18 ± 1	17 ± 1	16 ± 1	17 ± 1	10 ± 1†
HVP, mmHg	8 ± 1	12 ± 1*	14 ± 1	14 ± 1	14 ± 1	13 ± 1	11 ± 1	13 ± 1	7 ± 1†
PVP – HVP, mmHg	2.2 ± 0.6	6.2 ± 1.2*	4.7 ± 1.1	4.8 ± 1.1	5.8 ± 1.2	5.4 ± 1.1	5.6 ± 1.5	4.5 ± 0.9	2.2 ± 0.8†
IAP, mmHg	5.4 ± 0.6	16.0 ± 0.8*	15.8 ± 0.9	16.8 ± 1.1	16.0 ± 0.6	14.9 ± 0.3	14.5 ± 0.5	15.3 ± 0.7	4.1 ± 0.4†
CO, l/min	2.3 ± 0.2	2.6 ± 0.2	2.6 ± 0.1	2.7 ± 0.2	2.7 ± 0.2	2.4 ± 0.1	2.2 ± 0.1†	2.5 ± 0.1	2.1 ± 0.1†
HABF, ml/min	157 ± 27	234 ± 45*	236 ± 43	248 ± 42	217 ± 40	192 ± 30	181 ± 29	206 ± 33	146 ± 26†
PVBF, ml/min	734 ± 30	785 ± 42	835 ± 42	883 ± 50	812 ± 43	737 ± 33	685 ± 31‡	796 ± 38	719 ± 34
THBF, ml/min	891 ± 41	1,018 ± 76	1,072 ± 67	1,131 ± 68	1,029 ± 63	929 ± 46	866 ± 46	1,002 ± 52	865 ± 51

Values are means ± SE. \*  $P < 0.05$  between H4 (CO<sub>2</sub> insufflation, horizontal position) and H3 (no insufflation, horizontal position); †  $P < 0.05$  between H7 (exsufflation, horizontal position) and H6 (CO<sub>2</sub> insufflation, horizontal position); ‡  $P < 0.05$  vs. H5 (horizontal after head-down tilt).

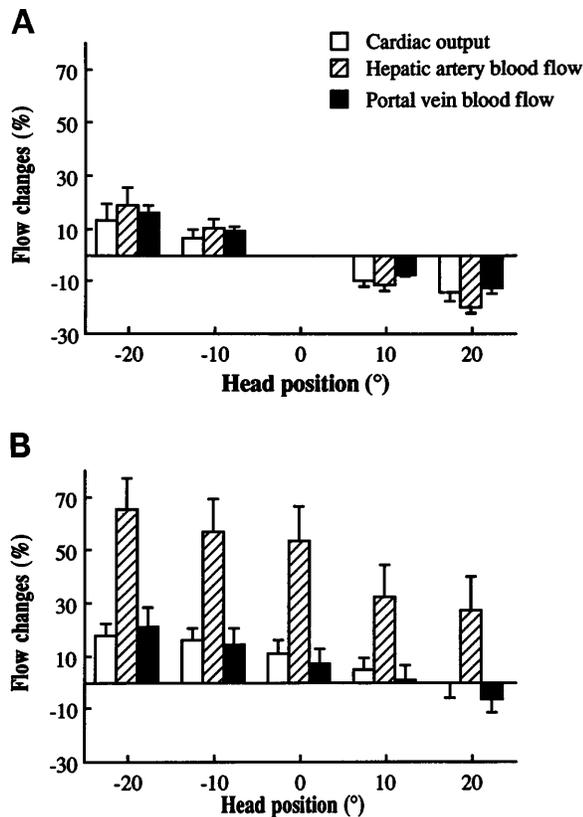


Fig. 1. Changes (%) of cardiac output, hepatic artery blood flow, and portal vein blood flow during changes of tilt in absence (A) and in presence (B) of pneumoperitoneum. 0°, Horizontal position; -20° and -10°, head-down tilts; 10° and 20°, head-up tilts. A: baseline value is value obtained before changes of tilt. B: to assess effect of CO<sub>2</sub> insufflation ± changes of tilts, baseline value was obtained before CO<sub>2</sub> insufflation (H3). During pneumoperitoneum, intra-abdominal pressure ranged from 14.5 to 16.8 mmHg.

insufflation increases HABF with no effect on THBF. The combination of CO<sub>2</sub> insufflation and head-down tilt has a beneficial effect on hepatic perfusion, whereas when the pneumoperitoneum is associated with the head-up tilt THBF is not modified. Consequently, the combination of CO<sub>2</sub> insufflation and changes in position do not compromise hepatic blood flow in our model, suggesting that hepatic blood flow may be preserved during laparoscopy if tilt does not exceed 20° and if the

IAP increase induced by CO<sub>2</sub> insufflation remains <15 mmHg.

Controversial results have been published about the modification of hepatic and mesenteric blood flows during elevated IAP. In early studies, IAP was increased by infusing balanced salt solutions (4, 5) or by inflating bags (3, 21) in the abdomen to mimic the increased IAP observed in massive ascites, bowel distension, abdominal bleeding, or omphalocele in newborns. Two recent studies used a pneumoperitoneum to increase IAP, but the gas insufflated was either CO<sub>2</sub> (11) or helium (2). In anesthetized pigs, Diebel et al. (5) showed that the IAP increase (induced by fluid infusion in the abdomen) may cause significant impairment of hepatic perfusion. Despite normal MAP and cardiac output, PVBF and HABF fell to 65 and 45%, respectively, of the baseline value at an IAP of 20 mmHg. When IAP reached 40 mmHg, cardiac output also decreased and hepatic hypoperfusion worsened. Mesenteric blood flow also decreased when IAP reached 20 mmHg (2-4). In contrast, in anesthetized dogs, increasing IAP up to 20 mmHg did not compromise mesenteric perfusion (16). When intraperitoneal pressure was increased up to 25 mmHg by inflating a large bag into the peritoneum, HABF increased and PVBF decreased but the increase in HABF was not sufficient to maintain THBF (21). Finally, when IAP was increased by CO<sub>2</sub> insufflation in anesthetized dogs, PVBF decreased but HABF was maintained (11). The various types of animals used for the studies (dogs, neonatal lambs, and pigs) may explain these conflicting results. Moreover, anesthesia was maintained by either pentobarbital (2, 11, 21) or isoflurane (5). The volemic status of the animals also interferes in the relationship between hemodynamic variables and IAP. Increasing IAP to 40 mmHg decreases cardiac output by 53% in hypovolemic dogs and by 17% in normovolemic dogs but raises cardiac output by 50% in hypervolemic dogs (14). Consequently, cardiac output at an IAP of 15 mmHg remained steady (5) or decreased (2, 3, 11, 21), whereas in anesthetized pigs cardiac output was slightly increased when IAP was moderately increased (9, 18, 23). Thus in normovolemic animals, when IAP remains below 20 mmHg, systemic and hepatosplanchnic perfusion or hemodynamics are not compromised. Because

Table 4. Systemic and hepatic variables of oxygenation before and after CO<sub>2</sub> insufflation

	Pneumoperitoneum							
	Horizontal H1	Head Down 20°	Head Up 20°	Horizontal H3	Horizontal H4	Head down 20°	Head up 20°	Horizontal H6
systDO <sub>2</sub> , ml/min	303 ± 10	348 ± 24	263 ± 12	295 ± 21	342 ± 32	350 ± 18	301 ± 11	326 ± 13
pvDO <sub>2</sub> , ml/min	60 ± 3	75 ± 5	51 ± 3	65 ± 3	72 ± 4	84 ± 5	61 ± 3	72 ± 3
haDO <sub>2</sub> , ml/min	21 ± 4	25 ± 5	17 ± 3	22 ± 4	31 ± 6	33 ± 5	24 ± 4	28 ± 4
haDO <sub>2</sub> /thDO <sub>2</sub> , %	25 ± 4	24 ± 4	25 ± 4	24 ± 3	28 ± 3	27 ± 4	28 ± 3	28 ± 3
systV̇O <sub>2</sub> , ml/min	143 ± 5	143 ± 5	142 ± 6	147 ± 6	151 ± 9	146 ± 6	143 ± 6	146 ± 7
hepV̇O <sub>2</sub> , ml/min	14.1 ± 2.7	14.8 ± 2.7	13.1 ± 1.8	15.4 ± 2.7	12.7 ± 1.8	17.3 ± 1.4	12.7 ± 1.8	15.1 ± 2.0
hepLac, μmol/min	142 ± 26	139 ± 34	111 ± 23	157 ± 27	157 ± 31	193 ± 12	167 ± 17	113 ± 9

Values are means ± SE. systDO<sub>2</sub>, systemic O<sub>2</sub> delivery; thDO<sub>2</sub>, total hepatic O<sub>2</sub> delivery; haDO<sub>2</sub>, hepatic artery O<sub>2</sub> delivery; systV̇O<sub>2</sub>, systemic O<sub>2</sub> consumption; hepV̇O<sub>2</sub>, hepatic O<sub>2</sub> consumption; hepLac, hepatic lactate uptake.

in clinical studies the IAP increase remains  $<15$  mmHg (12, 13, 25, 27), we chose to maintain this amplitude of IAP  $\leq 15$  mmHg during CO<sub>2</sub> insufflation.

In our study, after CO<sub>2</sub> insufflation, cardiac output and PVBF did not change significantly but HABF increased (+49%). However, the HABF increase was insufficient to concomitantly increase THBF. Because we used CO<sub>2</sub> insufflation to produce the pneumoperitoneum, we increased both IAP and CO<sub>2</sub> content in the abdomen. Besides the fact that increased IAP may modify regional blood flows, low pH and high PCO<sub>2</sub> in the portal vein may increase HABF and decrease PVBF (7). In our study, the greatest changes in pH and PCO<sub>2</sub> in the portal vein were  $7.35 \pm 0.02$  and  $53.5 \pm 2.1$  mmHg, respectively. Because these changes were lower than those necessary to modify hepatic blood flow (7), we postulated that variations of pH and PCO<sub>2</sub> had a minor effect on hepatic flow in our study. Further studies in which helium instead of CO<sub>2</sub> would be used at a similar IAP level might confirm this assumption. Because we continuously infused pigs with fluid during the protocol ( $8 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ ), we speculated that our pigs were normovolemic. The slight increase in cardiac output (+17%) observed during CO<sub>2</sub> insufflation is unlikely to be the consequence of hypercapnia because we maintained a normal PaCO<sub>2</sub>. Direct stimulation of intra-abdominal receptors induced by intraperitoneal distension or increased abdominal CO<sub>2</sub> concentration may cause this cardiac output increase (20). Moreover, blood volume is limited in pig lower extremities and a large blood volume is unlikely to be sequestered in the lower part of the body during CO<sub>2</sub> insufflation. In human studies, cardiac output is either unchanged (25, 26), increased (15), or decreased (8, 12, 13) during pneumoperitoneum. Besides the volemic status and levels of IAP, rates of CO<sub>2</sub> insufflation and time intervals between insufflation and data collection may explain the various evolution of cardiac output in human studies.

Besides the pneumoperitoneum, changes in position facilitate access to organs in the upper or lower part of the abdomen during laparoscopy. Before CO<sub>2</sub> insufflation, when pigs were positioned in the head-down tilt PVBF increased, but when they were in the head-up tilt both hepatic flows decreased. The changes in THBF followed the changes in cardiac output. The combination of CO<sub>2</sub> insufflation and changes in position, as observed in clinical practice, had a beneficial effect on hepatic perfusion in the head-down tilt, whereas THBF was similar in the horizontal position without pneumoperitoneum and in the head-up tilt during CO<sub>2</sub> insufflation. In anesthetized patients, progressive increases in IAP to 20 cmH<sub>2</sub>O increased cardiac output in both horizontal and head-down tilts (15). This result was not confirmed in healthy women who underwent laparoscopic hysterectomy in which the combination of anesthesia, head-down tilt, and pneumoperitoneum decreased cardiac output (8). In awake volunteers, the head-down tilt increased the cardiopulmonary blood volume with a concomitant cardiac output increase (19). Joris et al. (13) showed that the combination of anesthesia, head-up tilt, and pneumoperitoneum pro-

duced a 50% decrease in cardiac output in healthy patients during laparoscopic cholecystectomy. No information is available on the modifications of hepatic blood flow during clinical laparoscopy. Our results suggest that the combination of CO<sub>2</sub> insufflation and changes of position in normovolemic patients does not compromise hepatic blood flow.

Besides the changes in position and the increased IAP, other parameters may also interfere with the hepatic circulation during laparoscopy, such as the type of anesthesia and the minute ventilation. Pancuronium and fentanyl (6) do not significantly affect the hepatic blood flow. Because the effect of pentobarbital remains more controversial (6), anesthetic drugs were continuously infused to avoid major effects of anesthesia on hepatic perfusion. We must also consider that THBF has been altered by increasing the tidal volume to maintain PaCO<sub>2</sub> constant, through an increase in intrathoracic pressures after the increase in intra-abdominal pressures (22, 24). CO<sub>2</sub> insufflation also increased HVP, PVP, and the difference PVP – HVP, and these modifications of pressure around the liver might transfer blood volume from the hepatosplanchnic region to the chest and increase cardiac output (1, 30).

$\dot{V}_{\text{CO}_2}$  immediately increases after CO<sub>2</sub> insufflation and remains steadily elevated during the pneumoperitoneum, as previously described in a similar animal model (9). The fact that  $\dot{V}_{\text{CO}_2}$  does not increase with nitrogen (10) or helium (17) insufflation demonstrates that CO<sub>2</sub> absorption from the abdominal cavity largely contributes to this increased  $\dot{V}_{\text{CO}_2}$ . Changes in metabolic activity are not involved, because  $\dot{V}_{\text{O}_2}$  did not change as already shown (9). Moreover, no evidence of hypoxia might explain the elevated  $\dot{V}_{\text{CO}_2}$ , because systemic and hepatic variables of oxygenation remained unchanged during the study.

In summary, the combination of CO<sub>2</sub> insufflation and changes in position did not compromise hepatic blood flow in our model of anesthetized pigs, suggesting that hepatic blood flow may be preserved during laparoscopy if tilt does not exceed 20° and if the IAP increase following CO<sub>2</sub> insufflation remains  $<15$  mmHg. This study also points out all the parameters that interfere with the hepatic perfusion. Increased ventilation to maintain a normal PaCO<sub>2</sub>, head-up tilt, anesthetic drugs, and high PCO<sub>2</sub> in the portal vein may decrease hepatic perfusion, whereas head-down tilt and CO<sub>2</sub> insufflation have positive effects. All these parameters, including the volemic status of the patients, must be taken into consideration when performing surgical laparoscopy in patients suffering from patent or unknown diseases.

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