The association between central venous pressure, pneumoperitoneum, and venous carbon dioxide embolism in laparoscopic hepatectomy

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Abstract

Background   Laparoscopic hepatectomy (LH) is increasingly used. However, the safety and outcomes of LH have yet to be elucidated. The risk of venous gas embolism is increased during liver parenchymal transection. This risk may be increased with positive pressure carbon dioxide (CO_2) pneumoperitoneum (PP). This may be exacerbated further when low central venous pressure (CVP) anesthesia is used to minimize hemorrhage during liver resection.

Methods   To determine the risk of CO_2 venous embolism, hand-assisted laparoscopic left hepatic lobectomy was performed for 26 domestic pigs. They were divided into three groups involving, respectively, positive gradient (normal-pressure PP of 12–14 mmHg and low CVP of 5–7 mmHg), negative gradient (low-pressure PP of 7–8 mmHg and normal CVP of 10–12 mmHg), and neutral gradient (normal-pressure PP and normal CVP or low-pressure PP and low CVP). Transesophageal echocardiography (TEE) was used intraoperatively to assess the presence of emboli in the suprahepatic vena cava and the right side of the heart. The TEE was recorded and analyzed by blinded observers. Carbon dioxide embolism also was monitored using end-tidal CO_2 and compared with TEE.

Results   Carbon dioxide embolism was demonstrated in 19 of the 26 cases. The majority of gas emboli were small gas bubbles associated with dissection of the major hepatic veins. No statistically significant difference in the occurrence of gas emboli was observed between the groups. Of the 19 animals, 18 experienced no significant hemodynamic changes. One pig in the positive gradient group experienced hypotension in relation to gas embolism. The effects were only transient and did not preclude safe completion of the operation.

Conclusions   Carbon dioxide embolism during LH occurs frequently. Clinically, this finding appears to be nominal, but care must be taken when dissection around large veins is performed, and awareness by the surgical and anesthesiology teams of potential venous air embolism is essential. Further evaluation of this phenomenon is required.

Keywords   Central venous pressure · Embolism · Hepatectomy · Laparoscopy · Pneumoperitoneum

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Minimally invasive surgery in the abdomen saw rapid expansion from the 1990 s to the early part of this millennium. The evolution of laparoscopic hepatectomy (LH) has taken much longer. In fact, only a few centers remain in which the laparoscopic approach to liver resection is considered the primary approach for all hepatectomies. There are many reasons for this. Chief among them is the need to obtain oncologic results and perioperative complication rates similar to those for the open technique [1, 2].

Many reports currently describe a safety profile for LH comparable with that for case controls or historic controls in large case series that have not shown an increased morbidity or mortality rate [3–6]. Laparoscopic hepatectomy has gained general acceptance despite the absence of a randomized clinical trial, and it is unlikely that an

adequately powered trial will ever be conducted. Therefore, definitive answers to questions regarding the safety of LH will need to be studied in animal models that can be directly extrapolated to humans.

Blood loss during liver resection can be a technical challenge. A number of maneuvers are used to reduce the blood loss during liver parenchymal transection. Low central venous pressure (CVP) anesthesia has proved to be a safe and widely used technique to decrease blood loss [7, 8]. In open liver resection, the risk of air embolism with low CVP is increased, but with a low incidence of clinically relevant emboli manifested by hypotension or cardiac arrhythmia [9].

During laparoscopy, positive pressure insufflation of the peritoneal cavity using carbon dioxide (CO_2) is necessary to allow visualization. Significant air embolism has been reported with a variety of laparoscopic procedures [10]. The combination of low CVP and positive pressure pneumoperitoneum during laparoscopic liver parenchymal transection could result in catastrophic air emboli. We hypothesize that the pressure gradient between the insufflation pressure and the CVP will have a direct impact on the magnitude of air embolism.

Materials and methods

The research protocol was approved by The University of Western Ontario Council on Animal Care, the animal use subcommittee, and the Research Ethics Board (2004-013-02).

To evaluate the relationship between CVP, pneumoperitoneum, and venous air embolism, we performed a pilot study with 26 selected female domestic piglets weighing 50 to 70 kg, organizing them into four experimental arms: group 1 with a positive gradient (normal-pressure pneumoperitoneum, 14 mmHg; low CVP, ≤ 5 mmHg; $n = 7$), group 2 with a negative gradient (low-pressure pneumoperitoneum, 7 mmHg; normal CVP, 10–12 mmHg; $n = 7$), and group 3 with a neutral gradient (pneumoperitoneum pressure equal to CVP) including group 3a (normal-pressure pneumoperitoneum, 14 mmHg; normal CVP, 10–12 mmHg; $n = 6$) and group 3b (low-pressure pneumoperitoneum, 7 mmHg; low CVP, ≤ 5 mmHg; $n = 6$).
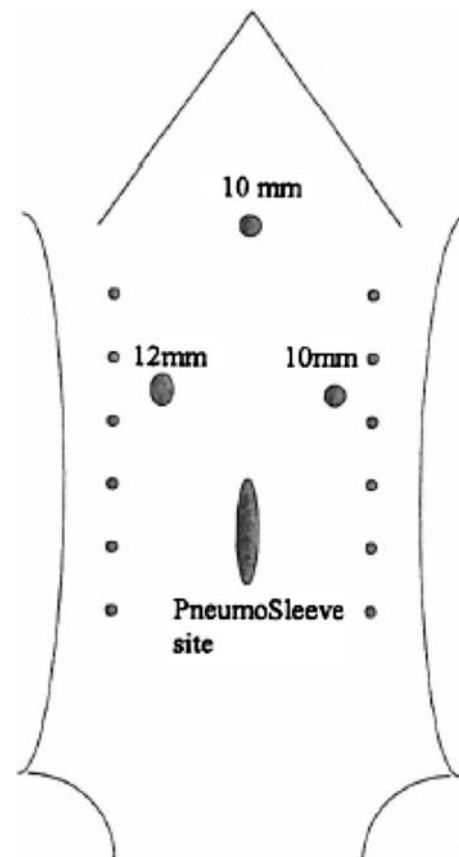
The pigs were fasted overnight, administered general anesthesia, and mechanically ventilated. The right internal jugular vein was cannulated by cutdown. Central venous pressure was maintained at target levels using a combination of crystalloid, diuretics, and vasopressors (epinephrine).

Transesophageal echocardiography (TEE) was used intraoperatively to determine the presence of air embolism in the suprahepatic vena cava and the right atrium. The TEE was placed preoperatively and recorded on videotape. The cassettes were reviewed postoperatively by blinded

observers. The results were graded according to the schema proposed by Schmandra et al. [11]. Carbon dioxide embolism also was monitored using end-tidal CO_2 measurements, which were compared with the TEE.

A hand port was placed followed by insertion of the remaining laparoscopic trocars (Fig. 1).The appropriate CO_2 pneumoperitoneum was obtained. The pigs were placed in the reverse Trendelenburg position. Ligation of the left hepatic artery was performed with metal hemoclips. A left hepatic lobectomy was performed. The hepatic parenchyma was divided along a line illustrated in Fig. 2.We used the harmonic scalpel (Ultracision, Ethicon, Cincinnati, OH) for parenchymal dissection. Vascular and biliary tributaries were controlled using a combination of harmonic scalpel, endoclips, endovascular staplers, and sutures. Larger structures such as the left pedicle and the hepatic vein or veins were controlled using endovascular staplers.

Other recorded parameters included operative time, blood loss, blood pressure, and heart rate. In addition, any significant electrocardiogram (ECG) changes were documented. Statistical analysis was performed using the Student's t-test and chi-square analysis.

Fig. 1 Schema of port placement on the pig ventral body surface

Line of resection

Fig. 2 Intrahepatic structures of the pig's liver (*visceral view*), with the vena cava seen in the caudate lobe and proposed line of resection

Results

Postoperative analysis of the TEE taped recordings demonstrated air embolism in 19 of the 26 cases. All cases of air embolism were stage 2 emboli according to Schmandra's classification system (gas emboli filling less than half the diameter of the right atrium, right ventricle, and right ventricular outflow tract) [11]. In the majority of cases, the emboli comprised small bubbles of gas occurring during parenchymal transection and were more pronounced toward the end of the case. This coincided with dissection of the major left hepatic vein tributaries. No statistically significant differences were detected in the incidence of air emboli between the groups.

Of the 19 cases in which emboli were noted, 18 of the subjects did not experience any significant hemodynamic changes (Table 1).One pig in the positive gradient group experienced hypotension in relation to gas embolism, but the effects were only transient and did not preclude safe completion of the operation. This animal did not experience any alteration of its end-tidal CO_2, nor did it experience any other operative complications such as increased blood loss. There was no difference in the operative blood loss between the groups. We did not detect any change in end-tidal CO_2 measurements with any of the procedures, even during the intraoperative appearance of CO_2 emboli on TEE.

Discussion

To date, the effect of alterations in CVP and insufflation pressure on the incidence and significance of venous air embolism during LH has not been studied. Our results demonstrate that there is no significant increase in the risk of air embolism with alteration of the CVP relative to the pressure of the pneumoperitoneum.

The need for expertise in two technically demanding subspecialities, namely, advanced laparoscopy and hepatobiliary surgery, has contributed to the gradual evolution of LH. The development of surgical technique and instruments has brought us to the current state, with LH performed more frequently, particularly for left lateral segmentectomy and segmentectomies or wedge excisions in the inferior and anterior portions of the liver [12].

However, major liver resection is performed only at a small number of centers and implemented as a routine approach at even fewer centers [13–15]. One main concern of surgeons is control of intraoperative hemorrhage during LH [16]. Low CVP anesthesia is widely practiced in open liver resection, with the clear benefit of reduced blood loss [7, 8]. When low CVP anesthesia is used laparoscopically, there is a theoretic increased risk of CO_2 embolism at insufflation pressures exceeding the CVP, which cause a pressure gradient in the venous circulation [17].

In addition, positive pressure pneumoperitoneum can further accentuate this gradient by altering the intrahepatic hemodynamics, which would not be reflected in the CVP. Other influences on this gradient include pretransection ligation of ipsilateral vessels, use of inflow occlusion or other techniques of vascular control, and patient positioning. Interestingly, positive pressure pneumoperitoneum has been shown to decrease blood loss from liver trauma in an animal model [18]. The counterpressure exerted by pneumoperitoneum can contribute to hemostasis during LH by tamponade [19].

Table 1 Comparison of clinical outcomes between groups

Group	No. of animals	No. of cases showing air emboli	Animals experiencing significant hemodynamic changes	No. of cases with decreased end-tidal CO_2	Mean blood loss ml (range)
1	7	5	1	0	200 (75–1200)
2	7	5	0	0	175 (50–300)
3a	6	5	0	0	190 (50–225)
3b	6	4	0	0	225 (125–400)

Schmandra et al. [20] reported a 100% incidence of CO_2 embolism detected by TEE in seven pigs that underwent laparoscopic left hepatectomy. The pneumoperitoneum/CVP gradient was not controlled in this study. Significantly, four of the animals experienced cardiac arrhythmias in association with the CO_2 embolism.

Conversely, in one of the early clinical reports, Farges et al. [21], using crude measures of venous CO_2 embolism, reported no gas embolism in 21 patients undergoing LH. Many subsequent case series have not demonstrated clinically relevant CO_2 embolism. Only a few reports have included data using TEE, which is arguably the most sensitive method for detecting gas embolism. We chose to analyze the recorded TEE tapes after the procedures, which allowed us to scrutinize the embolic events more closely than an anesthesiologist intraoperatively.

The occurrence of CO_2 embolism is likely dependent on many variables. Duration and size of parenchymal transection likely are directly proportional to the risk of gas embolism. Surgical technique and instrumentation also may play a role. Some types of instrumentation used to divide the liver parenchyma may increase this risk, as shown by a recent report describing a significantly higher risk of embolism in a small number of experimental animals when a vessel-sealing system was used [22]. A hand-assisted technique was shown to decrease the risk of embolism compared with a totally laparoscopic approach. Schmandra et al. [20] performed total LH on seven pigs and used hand-assisted LH on seven pigs. They found that air embolism occurred in five animals of the total LH group, with significant cardiac arrhythmia in three of the animals. None of the pigs in the hand-assisted group experienced any air emboli [20]. The findings of these authors are in contrast to ours, which show that 19 of 26 pigs experienced air embolism with the hand-assisted technique.

In addition, gas emboli with the use of argon plasma coagulation have been reported. The risk of embolism is increased with a rapid increase in the intraperitoneal pressure and because argon is 17 times less soluble than CO_2 in the blood. It is possible that the hemodynamic and physiologic differences between pigs and humans in response to pneumoperitoneum could result in different hemodynamic consequences in humans. Pigs are not a perfect model for human response to pneumoperitoneum, but dogs and other animals appear to be no better [23].

The largest published experience with LH in humans comes from two academic centers in the United States. This experience demonstrated only one episode of CO_2 embolism, which caused transient hemodynamic instability in a series of 335 resections [24].

In our experimental model, the use of lower insufflation pressures did not impair visualization. In addition, we did not detect increased blood loss in the low-pressure pneumoperitoneum groups (groups 3 and 3b). Our data demonstrated transient episodes of gas embolism in the majority of cases we managed. These episodes typically occurred during dissection near the left hepatic vein in our experiment. The emboli tended to cease at division of the left hepatic vein. In many cases, we also noted tiny, transient, subclinical emboli during parenchymal dissection. We did not observe a statistical difference in the number of animals that experienced embolic events detected by TEE between the study groups, but it is worth noting that the only animal that experienced hemodynamic compromise was in the positive gradient group (group 1).

These data suggest that embolism of small bubbles are not likely to cause hemodynamic consequences and should be rapidly absorbed due to the solubility of CO_2 in the plasma. However, large bubbles may cause a gas lock and can lead to pulmonary vascular outflow obstruction. Due to the small sample sizes in this study and the potentially catastrophic results of gas embolism, further study is recommended.

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