

Perioperative management of patients with increased risk of laparoscopy-induced hepatic hypoperfusion

François Clergue, Philippe Morel, Catherine M. Pastor

Départements de Chirurgie et d'Anesthésie, Hôpitaux Universitaires de Genève, Geneva, Switzerland

Summary

Because hepatic hypoperfusion induced by laparoscopy has been underestimated, the aim of this article is to review the numerous factors influencing hepatosplanchnic blood flow during laparoscopy and to alert clinicians to the adverse

consequences of hepatic hypoperfusion in high risk patients undergoing this procedure.

Key words: laparoscopy; hepatic circulation; human studies; experimental studies; high-risk patients

Introduction

Indications for laparoscopic versus open surgery have rapidly widened, since the technique shortens postoperative recovery time and reduces postoperative complications [1–3]. Well-accepted indications for laparoscopy are cholecystectomy and diagnostic procedures such as evaluation of abdominal pain and haemorrhage and staging of malignant tumours [3]. Appendicectomy, exploration of the common bile duct, repair of inguinal hernia, colon resection, surgery for gastro-oesophageal reflux and peptic ulcer disease are gaining acceptance. Many other laparoscopic procedures are performed as technical limitations are addressed by numerous investigators and manufacturers.

During laparoscopy, a working space to facili-

tate surgery is established by continuously insufflating an inert gas in the peritoneal cavity whose volume should be large enough to facilitate surgery without increasing intra-abdominal pressure (IAP) over a threshold limit (usually 15 mm Hg). The most commonly used gas is CO₂, since it permits safe electrocautery and is rapidly absorbed and dissolved into vessels, thus minimising the risk of gas embolism. Potential complications described during intra-abdominal CO₂ insufflation include abdominal injuries and cardiovascular and respiratory disorders, which are easily avoided in low-risk patients undergoing short-time surgery. However, while the procedure is gaining acceptance among general surgeons, laparoscopy is now performed in high risk patients, including elderly patients with pre-existing cardiovascular diseases, patients with hepatic dysfunction and critically ill patients.

Because hepatic hypoperfusion induced by laparoscopy has been underestimated, the aim of this article is to review the numerous factors influencing hepatosplanchnic blood flow during laparoscopy (table 1) and to alert clinicians to the adverse consequences of hepatic hypoperfusion in high-risk patients undergoing this procedure.

Table 1

Factors influencing hepatic perfusion during laparoscopy.

	References
Increased intra-abdominal pressure	1, 4–15
Dysregulation of hepatic arterial buffer response	16
Changes of position	17–21
Anaesthetic technique	22
Volaemic status	21, 23
Effects of pH and pCO ₂	21, 27, 28

Pathophysiology of laparoscopy-induced hepatic hypoperfusion

Increase in intra-abdominal pressure (IAP)

Few studies have investigated the consequences of intraabdominal CO₂ insufflation on hepatosplanchnic perfusion. In healthy patients undergoing cholecystectomy and appendicectomy,

Schilling et al. [4] measured the microcirculation of abdominal organs by introducing a laser Doppler into the peritoneum through a 5-mm trocar. During CO₂ insufflation (IAP = 15 mm Hg) there was a significant decrease in the gastric

(-53%), duodenal (-11%), jejunal (-32%), colonic (-44%), hepatic (-39%), and peritoneal (-60%) microcirculations. By inserting a pulsed Doppler ultrasonic probe through the umbilicus, Takagi [5] also showed that portal vein blood flow decreased when IAP was ≥ 10 mm Hg in a similar group of patients. The decreased blood flow is proportional to the increase in IAP [6]. Finally, in healthy elderly patients Sato et al. [7] assessed hepatic blood flow by transoesophageal Doppler echography of the hepatic vein during cholecystectomy, and showed that hepatic perfusion is significantly altered while the hepatic blood flow was well maintained during open cholecystectomy.

In experimental studies, numerous but controversial results have been published concerning the modification of hepatic and mesenteric blood flows during elevated IAP. Experimental designs are likely to be responsible for these controversies. In early studies, IAP was increased by infusing balanced salt solutions [8, 9] or by inflating bags [10, 11] in the abdomen to mimic the increased IAP observed in massive ascites, bowel distention, and omphalocele in newborns. Recent studies have used a pneumoperitoneum to increase IAP to mimic laparoscopy, but the gas insufflated was either CO₂ [12] or helium [13]. In anaesthetised pigs, Diebel et al. [8] showed that increased IAP impairs hepatic perfusion. In this study, despite the steady mean arterial pressure and cardiac output measured during the procedure, portal vein blood and hepatic artery blood flows fall to 65% and 45% of the baseline value respectively at an IAP of 20 mm Hg. When IAP reached 40 mm Hg, cardiac output also decreases and hepatic hypoperfusion worsens. Mesenteric blood flow also decreases when IAP increases up to 20 mm Hg [9, 10, 13]. In contrast, in anaesthetised dogs and pigs, increasing IAP up to 20 mm Hg [14] or 12 mm Hg [15] does not compromise mesenteric perfusion. Finally, when IAP is increased by CO₂ insufflation in anaesthetised dogs, portal vein blood flow decreases but hepatic artery blood flow is maintained [12].

Because portal vein blood and hepatic artery blood flows may be differently regulated during abdominal CO₂ insufflation, several experimental studies have investigated the "hepatic arterial buffer response" which is defined as the inverse change in hepatic arterial resistance in response to modification of portal vein blood flow. Thus, in physiological conditions, hepatic artery blood flow increases to compensate for a decrease in portal vein blood flow to maintain constant hepatic perfusion. Richter et al. [16] recently showed that in anaesthetised rats the hepatic arterial buffer response was altered during intra-abdominal CO₂ insufflation, a fact which may represent a further risk factor for hepatic hypoperfusion during laparoscopy.

Although interspecies differences may explain the controversial effects of IAP increase on hepatic blood flow, it is possible to conclude that in exper-

imental models hepatic blood flow is either maintained or decreased, and that local regulation of hepatic and portal blood flows is impaired.

Changes of position

To increase the working space, head-down tilt position is used during intestinal surgery while head-up tilt position facilitates surgery in the esogastric area. Because in awake volunteers, head-down tilt increases the cardiopulmonary blood volume with a concomitant increase in cardiac output [17], the combination of intraabdominal CO₂ insufflation and head-down tilt may be more effective in preserving hepatic perfusion than the combination of head-up tilt position and intraabdominal CO₂ insufflation. In 1972, Kelman et al. [18] showed that a progressive increase in IAP up to 20 cm H₂O increases cardiac output in both the horizontal and head-down tilts. This result was not confirmed in healthy women who underwent laparoscopic hysterectomy. In this study, the combination of anaesthesia, head-down tilt and pneumoperitoneum decreases cardiac output [19]. Finally, Joris et al. [20] showed that the combination of anaesthesia, head-up tilt and pneumoperitoneum produces a 50% decrease in cardiac output in healthy patients during laparoscopic cholecystectomy. No information is available concerning modification of hepatic perfusion by a combination of position changes and intra-abdominal CO₂ insufflation in anaesthetised patients.

We showed that in anaesthetised pigs head-down tilt before CO₂ insufflation increases portal vein blood flow, while head-up tilt decreases both hepatic flows [21]. In this experimental model, the combination of CO₂ insufflation and changes in position had a beneficial effect on hepatic perfusion in the head-down tilt, whereas hepatic blood flow was not modified by the combination of head-up tilt and CO₂ insufflation. Further studies are therefore needed to obtain such information in humans.

Anaesthetic technique

Anaesthetic drugs and volaemic status also interfere with hepatosplanchnic perfusion. All drugs that decrease cardiac output produce proportional effects on hepatic blood flow. In addition, some anaesthetic agents have more specific effects on hepatic perfusion. For instance, while halothane increases hepatic arterial resistance, isoflurane increases regional blood flow. Other drugs such as pancuronium and fentanyl do not significantly affect hepatic blood flow [22]. Additionally, epidural anaesthesia may modify hepatic flow to an extent dependent on the block level.

Volaemic status

Volaemic status also interferes with haemodynamic variables. Increasing IAP up to 40 mm Hg decreases cardiac output by 53% in hypovolaemic dogs and by 17% in normovolaemic dogs, but raises cardiac output by 50% in hypervolaemic

dogs [23]. We have confirmed these results in normovolaemic pigs [21]. Since in clinical studies cardiac output is either unchanged [24, 25], increased [18] or decreased [19, 20, 26] during pneumoperitoneum, these conflicting findings may be explained by the volaemic status of anaesthetised patients.

Effect of pH and pCO₂

Low pH and high pCO₂ may modify hepatic blood flow during intra-abdominal CO₂ insufflation. Thus, CO₂ easily diffuses through the peritoneum, increasing blood pCO₂. Hypercarbic acidosis and its deleterious effects on cardiac output and regional circulation can easily be avoided by increasing ventilation. However, in patients with impaired cardiac output or pulmonary dysfunction, CO₂ transport from the peritoneal cavity to the lungs is slow and increased CO₂ retention must be detected. This is why several studies have assessed the consequences of insufflating different types of gas as well as the possibility of avoiding gas insufflation (abdominal-wall lift technique or retractor method) to limit the vascular effects of CO₂.

The consequences of high pCO₂ in blood have been investigated in experimental studies. Gelman et al. [27] showed that low pH and high pCO₂ increase hepatic arterial blood flow and reduce portal blood flow. In anaesthetised pigs we measured pH and pCO₂ in the portal vein during CO₂ insufflation and found minimal changes: pH and pCO₂ in the portal vein were 7.29 ± 0.02 and 8.50 ± 0.30 kPa respectively [21]. However, in this experimental model we modified mechanical ventilation to keep arterial pCO₂ within normal ranges. Because these changes were lower than those necessary to modify hepatic blood flow [27], we postulated that variations in pH and pCO₂ during laparoscopy had only a minor effect on hepatic blood flow [21]. Moreover, we recently showed that in isolated perfused rat livers metabolic and hypercarbic acidosis

has no effect on hepatic flow and on the response to increasing doses of norepinephrine [28]. Hence, in clinical practice, modifications of pH and pCO₂ in hepatic vessels should have little effect on hepatic blood flow.

Outcome

As shown in the previous sections, numerous factors modify hepatic perfusion and the consequences of such hypoperfusion on hepatic function and outcome need to be further investigated. Few studies have investigated hepatic tests after laparoscopic surgery. Saber et al. [29] compared hepatic enzyme release following uneventful open and laparoscopic cholecystectomy by day 2 after surgery. They found that alanine aminotransferases doubled in 58% of healthy patients who had undergone laparoscopy and in only 6% of those who had undergone open surgery. The results were similar for aspartate aminotransferases, and all values returned to baseline by day 7. Similar results were published by Tan et al. [30] and Andrei et al. [31]. Interestingly, Kotabe et al. [32] showed that the degree of hepatic injury may be higher in laparoscopic colectomy than in laparoscopic cholecystectomy. Because the increase in IAP was similar for the two surgical procedures, the increased injury in cholecystectomy may result from patient position. Another important proposition has recently been advanced in a rat laparoscopy model [33]. Preconditioning (a 10-min insufflation followed by a 10-min deflation) may prevent the hepatic injury induced by a 60-min insufflation.

From these studies it may be concluded that in healthy patients undergoing laparoscopic surgery the transient hepatic hypoperfusion induced by laparoscopic surgery probably has no effect on hepatic function and outcome. However, hepatic enzyme release following long-lasting laparoscopy has never been published in large groups of patients. In these circumstances, prolonged hypoperfusion may be more deleterious [30].

Clinical implications in high risk patients

As stated previously, most publications on laparoscopic interventions involve young and healthy patients. With the rapid advances in laparoscopic technology and surgical skills the procedure is now performed in high risk patients, including elderly patients with pre-existing cardiovascular diseases, patients with hepatic dysfunction and critically ill patients. In these patients, the alterations in hepatic blood flow and hepatic functions are likely to be more deleterious than in healthy subjects. However, these questions have never been investigated.

It has long been known that postoperative complications and mortality within 30 days of surgery are high (30.1% and 11.6% respectively) in patients with cirrhosis undergoing all types of sur-

gical intervention under anaesthesia [34]. In contrast, several studies have recently emphasised the uneventful outcome of laparoscopy in patients with cirrhosis. In 25 consecutive patients with mild cirrhosis (Child A and B) who underwent laparoscopic cholecystectomy, all patients survived and the hospital stay (1.7 days) was similar to that observed in healthy patients [35]. Postoperative complications were haematomas (n = 3), ascites (n = 3), and pneumonia (n = 2). Patients with mild cirrhosis tolerate laparoscopic cholecystectomy nearly as well as those without cirrhosis [36]. Advantages of laparoscopic cholecystectomy over open surgery have also been shown by Poggio et al. [37]. Patients with mild cirrhosis tolerate laparoscopy better than open surgery (including lower mortality,

- 12 Ishizaki Y, Bandai Y, Shimomura K, Abe H, Ohtomo Y, Idezuki Y. Safe intraabdominal pressure of carbon dioxide pneumoperitoneum during laparoscopic surgery. *Surgery* 1993;114:549-54.
- 13 Bongard F, Pianim N, Dubecz S, Klein SR. Adverse consequences of increased intra-abdominal pressure on bowel tissue oxygen. *J Trauma* 1995;39:519-24.
- 14 Kleinhaus S, Sammartano R, Boley SJ. Effects of laparoscopy on mesenteric blood flow. *Arch Surg* 1978;113:867-9.
- 15 Blobner M, Bogdanski R, Kochs E, Henke J, Findeis A, Jelen-Esselborn S. Effects of intraabdominally insufflated carbon dioxide and elevated intraabdominal pressure on splanchnic circulation. *Anesthesiology* 1998;89:475-82.
- 16 Richter S, Olinger A, Hildebrandt U, Menger MD, Vollmar B. Loss of physiologic hepatic blood flow control ("hepatic arterial buffer response") during CO₂-pneumoperitoneum in the rat. *Anesth Analg* 2001;93:872-7.
- 17 London GM, Levenson JA, Safar ME, Simon AC, Guerin AP, Payen D. Hemodynamic effects of head-down tilt in normal subjects and sustained hypertensive patients. *Am J Physiol* 1983;245:H194-H202.
- 18 Kelman GR, Swapp GH, Smith I, Benzie RJ, Gordon NLM. Cardiac output and arterial blood-gas tension during laparoscopy. *Br J Anaesth* 1972;44:1155-62.
- 19 Hirvonen EA, Nuutinen LS, Kauko M. Hemodynamic changes due to Trendelenburg positioning and pneumoperitoneum during laparoscopic hysterectomy. *Acta Anaesth Scand* 1995;39:949-55.
- 20 Joris JL, Noirot DP, Legrand MJ, Jacquet NJ, Lamy ML. Hemodynamic changes during laparoscopic cholecystectomy. *Anesth Analg* 1993;76:1067-71.
- 21 Klopfenstein CE, Morel DR, Clergue F, Pastor CM. Effects of abdominal CO₂ insufflation and changes of position on hepatic blood flow in anesthetized pigs. *Am J Physiol* 1998;275:H900-H905.
- 22 Gelman S, Dillard E, Bradley EL. Hepatic circulation during surgical stress and anesthesia with halothane, isoflurane, or fentanyl. *Anesth Analg* 1987;66:936-43.
- 23 Kashtan J, Green JF, Parsons EQ, Holcroft JW. Hemodynamic effects of increased abdominal pressure. *J Surg Res* 1981;30:249-55.
- 24 Odeberg S, Ljungqvist O, Svenberg T, Gannedahl P, von Rosen A, Sollevi A. Haemodynamic effects of pneumoperitoneum and the influence of posture during anaesthesia for laparoscopic surgery. *Acta Anaesth Scand* 1994;38:276-83.
- 25 Odeberg S, Sollevi A. Pneumoperitoneum for laparoscopic surgery does not increase venous admixture. *Eur J Anaesth* 1995;12:541-8.
- 26 Johannsen G, Andersen M, Juhl B. The effect of general anesthesia on the haemodynamic events during laparoscopy with CO₂-insufflation. *Acta Anaesth Scand* 1989;33:132-6.
- 27 Gelman S, Ernst EA. Role of pH, PCO₂, and O₂ content of portal blood in hepatic circulatory autoregulation. *Am J Physiol* 1977;233:E255-E262.
- 28 Pastor CM, Hadengue A. Acidosis modifies metabolic functions but does not affect vascular resistances in perfused rat liver. *J Hepatol* 2001;34:507-13.
- 29 Saber AA, Laraja RD, Nalbandian HI, Pablos-Mendez A, Hanna K. Changes in liver function test after laparoscopic cholecystectomy: not so rare, not always ominous. *Am Surg* 2000;66:699-702.
- 30 Tan M, Xu FF, Peng JS, Li DM, Chen LH, Lv BJ, et al. Changes in the level of serum liver enzymes after laparoscopic surgery. *World J Gastroenterol* 2003;9:364-7.
- 31 Andrei VE, Schein M, Margolis M, Rucinski JC, Wise L. Liver enzymes are commonly elevated following laposcopic cholecystectomy: is elevated intra-abdominal pressure the cause? *Dig Surg* 1998;15:256-9.
- 32 Kotake Y, Takeda J, Matsumoto M, Tagawa M, Kikuchi H. Sub-clinical hepatic dysfunction in laparoscopic cholecystectomy and laparoscopic colectomy. *Br J Anaesth* 2001;87:774-7.
- 33 Yilmaz S, Koken T, Tokyol C, Kahraman A, Akbulut G, Serteser M, et al. Can preconditioning reduce laparoscopy-induced tissue injury? *Surg Endosc* 2003;17:819-24.
- 34 Ziser A, Plevak DJ, Wiesner RH, Rakela J, Offord KP, Brown DL. Morbidity and mortality in cirrhotic patients undergoing anesthesia and surgery. *Anesthesiology* 1999;90:42-53.
- 35 Sleeman D, Namias N, Levi D, Ward FC, Vozenilek J, Silva R, et al. Laparoscopic cholecystectomy in cirrhotic patients. *J Am Coll Surg* 1998;187:400-3.
- 36 Fernandes NF, Schwesinger WH, Hilsenberck SG, Gross GWW, Bay MK, Sirinek KR, et al. Laparoscopic cholecystectomy and cirrhosis: a case-control study of outcomes. *Liver Transpl* 2000;6:340-4.
- 37 Poggio JL, Rowland CM, Gores GJ, Nagorney DM, Donohue JH. A comparison of laparoscopic and open cholecystectomy in patients with compensated cirrhosis and symptomatic gallstone disease. *Surgery* 2000;127:405-11.
- 38 Villavicencio RT, Aucar JA. Analysis of laparoscopy in trauma. *J Am Coll Surg* 1999;189:11-20.
- 39 Brandt CP, Priebe PP, Eckhauser ML. Diagnostic laparoscopy in the intensive care patient. Avoiding the nontherapeutic laparotomy. *Surg Endosc* 1993;7:168-72.
- 40 Zollinger A, Krayer S, Singer T, Seifert T, Heinzelmann M, Schlumpf R, et al. Haemodynamic effects of pneumoperitoneum in elderly patients with increased cardiac risk. *Eur J Anaesthesiol* 1997;14:266-75.
- 41 Feig BW, Berger DH, Dougherty TB, Dupuis JF, Hsi B, Hickey RC, et al. Pharmacologic intervention can reestablish baseline hemodynamic parameters during laparoscopy. *Surgery* 1994;116:733-9.
- 42 Pastor CM, Morel DM, Clergue F, Mentha G, Morel P. Effects of abdominal CO₂ insufflation on renal and hepatic blood flows during acute hemorrhage in anesthetized pigs. *Crit Care Med* 2001;2001:1017-22.

The many reasons why you should choose SMW to publish your research

What Swiss Medical Weekly has to offer:

- SMW's impact factor has been steadily rising, to the current 1.537
- Open access to the publication via the Internet, therefore wide audience and impact
- Rapid listing in Medline
- LinkOut-button from PubMed with link to the full text website <http://www.smw.ch> (direct link from each SMW record in PubMed)
- No-nonsense submission – you submit a single copy of your manuscript by e-mail attachment
- Peer review based on a broad spectrum of international academic referees
- Assistance of our professional statistician for every article with statistical analyses
- Fast peer review, by e-mail exchange with the referees
- Prompt decisions based on weekly conferences of the Editorial Board
- Prompt notification on the status of your manuscript by e-mail
- Professional English copy editing
- No page charges and attractive colour offprints at no extra cost

Editorial Board

Prof. Jean-Michel Dayer, Geneva
 Prof. Peter Gehr, Berne
 Prof. André P. Perruchoud, Basel
 Prof. Andreas Schaffner, Zurich
 (Editor in chief)
 Prof. Werner Straub, Berne
 Prof. Ludwig von Segesser, Lausanne

International Advisory Committee

Prof. K. E. Juhani Airaksinen, Turku, Finland
 Prof. Anthony Bayes de Luna, Barcelona, Spain
 Prof. Hubert E. Blum, Freiburg, Germany
 Prof. Walter E. Haefeli, Heidelberg, Germany
 Prof. Nino Kuenzli, Los Angeles, USA
 Prof. René Lutter, Amsterdam, The Netherlands
 Prof. Claude Martin, Marseille, France
 Prof. Josef Patsch, Innsbruck, Austria
 Prof. Luigi Tavazzi, Pavia, Italy

We evaluate manuscripts of broad clinical interest from all specialities, including experimental medicine and clinical investigation.

We look forward to receiving your paper!

Guidelines for authors:

http://www.smw.ch/set_authors.html

Impact factor Swiss Medical Weekly



All manuscripts should be sent in electronic form, to:

EMH Swiss Medical Publishers Ltd.
 SMW Editorial Secretariat
 Farnsburgerstrasse 8
 CH-4132 Muttenz

Manuscripts: submission@smw.ch
 Letters to the editor: letters@smw.ch
 Editorial Board: red@smw.ch
 Internet: <http://www.smw.ch>