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Prospective assessment of the safety and benefit of laparoscopic liver resections

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Abstract
Background/Purpose. Laparoscopy represents an alternative to open surgery for virtually all digestive surgery procedures, with the anticipated short-term advantage of reduced esthetic prejudice, postoperative pain, and duration of in-hospital stay. In this study, we investigated the safety and benefits of laparoscopic liver resections in patients with benign solid liver tumors.
Methods. Laparoscopic liver resection of up to two segments for benign liver tumor was performed under continuous carbon dioxide (CO_2) pneumoperitoneum in 21 patients with no underlying chronic liver disease. The risk of gas embolism was assessed by end-tidal CO_2 and O_2 saturation, and the hemodynamic variations were monitored by a Swan-Ganz catheter. The postoperative course was compared with that following open surgery by matched-pair analysis.
Results. No patient experienced gas embolism or was converted, and clamping of the hepatic pedicle resulted in hemodynamic variations comparable to those observed during open surgery. Duration of surgery (177 vs 156 min.), intraoperative blood loss (218 vs 285 ml), modifications of postoperative liver function tests, and incidence of postoperative complications (10% vs 10%) were comparable to those after open surgery. Laparoscopic resection was associated with a 50% reduction (15.5 vs 31.6 mg) in morphine consumption during the first postoperative days, a reduction of the delay to oral intake of 0.8 days, and a reduction of in-hospital stay of 1.4 days.
Conclusions. Liver resections of up to two segments can be performed by laparoscopy using the same technique as that used during open surgery. However, the benefits observed compared with open surgery appear to be limited.

Key words Liver resection · Laparoscopy · Benign liver tumor · Hemodynamic monitoring · Prospective study · Comparative study

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Introduction

Laparoscopic liver resection was first reported in 1992,[1] at a time when laparoscopic surgeons were expanding their technique to virtually all abdominal surgical procedures. However, in contrast to other operations, where it has become a routine or the standard procedure,[2–4] laparoscopic hepatectomies are sill being performed in a very limited number of institutions worldwide, and the reported experience is scarce, with few studies of more than ten patients.[5–11] Indeed, liver surgery is being increasingly performed by specialized surgeons who are not necessarily trained in, or have routine practice with laparoscopic surgery. In addition, the main objective of liver surgeons is still to achieve a 0% in-hospital mortality rate, and any change in the current technique that would increase this risk is felt to be unacceptable.

Because we had expertise in both laparoscopic surgery[12,13] and open abdominal liver surgery,[14] we have launched a prospective evaluation of laparoscopic liver resections. This study reports our initial experience with the aim of assessing: (a) the risk of intraoperative bleeding and gas embolism; (b) the hemodynamic tolerance to clamping of the hepatic pedicle, and (c) the potential benefit of the laparoscopic approach compared with open surgery in patients with benign liver tumors.

Patients and methods

Selection of patients

Over a 2-year period, among 234 patients who underwent partial liver resection, 24 (10%) were offered the possibility to undergo this resection by laparoscopy and gave their informed consent. After exclusion of 3 patient with hepatocellular carcinoma, who have already been described,[15] 21 female patients, aged from 18 to 56

Table 1. Extent of hepatectomy and topography of the tumor in 42 patients undergoing resection of a benign liver tumor either by laparoscopy or by open surgery

	Laparoscopy	Open surgery
Tumorectomy		
No. of patients	9	9
Tumor diameter in cm; mean (range)	3.3 (3–4)	3.4 (2–5)
Segment 2, 3, or 4	4	3
Segment 5 or 6	3	4
Segment 7 or 8	2	2
Segmentectomy		
No. of patients	4	4
Tumor diameter in cm; mean (range)	4.5 (2–7)	4.7 (3–6)
Segment 3	1	0
Segment 4	0	2
Segment 5 or 6	3	2
Bisegmentectomy		
No. of patients	8	8
Tumor diameter in cm; mean (range)	7.3 (4–11)	5.9 (3–10)
Bisegmentectomy 5–6	2	0
Bisegmentectomy 4–5	0	1
Left lateral segmentectomy	6	7

years, who had presumed benign liver tumors developed in a normal liver were selected for the present study. The indication for resection was either the presence of symptoms ($n = 8$) or part of the diagnosis workup ($n = 13$). The topography of the tumor and extent of resection are summarized in Table 1. The size of the tumor ranged between 2.5 and 11 cm (mean, 4.9 cm). Analysis of the resected specimens showed the presence of focal nodular hyperplasia in 17, adenoma in 2, and hemangioma in 2. Five of these patients had mild steatosis.

Technique of laparoscopic resection

Patients were operated on under continuous CO_2 pneumoperitoneum at a pressure ranging between 10 and 15 mmHg, and not exceeding this pressure to avoid gas embolism, using five to six disposable trocars. Liver resections were performed in exactly the same way as during open liver surgery, except that the ligamentum teres was never divided and that the division of the falciform ligament was not necessary, except during left lateral segmentectomies. The portal pedicle was systematically encircled with a tape passed in a 24 Fr, 4-cm-long, rubber tube that was left free in the peritoneal cavity so as to allow a Pringle maneuver to be performed if required. The line of liver transection was marked on the liver surface by diathermy. The liver parenchyma was transected with an ultrasonic dissector (Dissectron; Satelec Medical, Merignac, France). Small vascular or biliary radicles were divided after bipolar coagulation or between endoclips. In the six patients undergoing a left lateral segmentectomy, the portal pedicles to segment 2 and 3 were transected extraparenchymally with an endo stapler (endo GIA30; Autosuture, Ethicon, France). Four of these patients had a common trunk between the left and median hepatic vein. This trunk was dissected extraparenchymally to allow lateral clamping during transection, if required, and the left hepatic vein was transected intraparenchymally. In the two other patients, the left hepatic vein was controlled and transected extraparenchymally. Biliostasis was assessed in 12 patients who had undergone either a segmentectomy or a bisegmentectomy, by methylene blue injection in the cystic duct following cholecystectomy. The cut surface was subsequently sealed with fibrin glue, using a disposable laparoscopic device. The resected liver was removed into an endopouch via a Pfannenstiel incision or the enlarged incision of a trocar, according to the size of the specimen. Aspirative abdominal drainage was not systematically used.

Intraoperative monitoring

The intraoperative endpoints assessed were the hemodynamic variations, the incidence of gas embolism, blood loss, and duration of surgery. In the first ten patients, a Swan-Ganz catheter was systematically inserted for continuous intraoperative hemodynamic monitoring of the systemic arterial pressure (SAP), central venous pressure (CVP), wedge pulmonary pressure (WPP), and cardiac outflow. Data were recorded prior to CO_2 insufflation, as well as prior to and 5 min after clamping of the hepatic pedicle. In the other 11 patients undergoing laparoscopic hepatectomy, invasive intraoperative hemodynamic monitoring was not routinely used. The risk of intraoperative gas embolism was systematically assessed by end-tidal CO_2 and O_2 saturation, as well as, in the first 4 patients, by transesophageal cardiac ultrasound. Intraoperative blood loss was accurately quantitated by subtracting, from the amount of fluid aspirated, the volume of fluid that had been instilled through the irrigation or the ultrasonic dissector. Duration of surgery was the time elapsed between trocar insertion and abdominal wound closure.

Postoperative monitoring

The postoperative endpoints assessed were the incidence of postoperative complications, delay to semisolid oral intake, analgesia requirement between postoperative days 1 and 3, postoperative kinetics of liver function tests, and duration of in-hospital stay. Postoperative pain was relieved by morphine and acetaminophen, and the nursing staff was encouraged to give analgesia as necessary, using a visual analogue scale.

The results of intraoperative hemodynamic monitoring and the incidence of gas embolism in patients operated by laparoscopy were compared with data obtained in patients who had been prospectively monitored using the same protocol for the purpose of a controlled study of vascular clamping during open surgery.[16,17] Intraoperative blood loss, duration of surgery, and postoperative course in patients undergoing laparoscopic surgery were compared with that achieved after open liver resection by a matched-pair analysis. Using an ongoing database, each of the 21 patients in the study group was blindly matched with one patient who had undergone open liver surgery for a benign liver tumor during the past 5 years, for age (38 ± 9 vs 39 ± 8 years), sex, and size and topography of the tumor, as well as type of liver resection performed (Table 1) and body mass index (24 ± 5 vs 23 ± 5 kg/m^2).

Statistical analysis

Comparison of variables was performed using the Student's *t*-test, Mann-Whitney *U*-test, or Fisher's exact test as required.

Results

Hemodynamic study

Insufflation of CO_2 into the abdomen resulted in a decrease in CVP (from 10.5 ± 2.3 to 9.3 ± 4.6 mmHg) and WPP (from 11.1 ± 3.0 to 9.1 ± 6.2 mmHg), an increase in SAP (from 86 ± 16 to 104 ± 20 mmHg), and no change in cardiac outflow (5.8 ± 1.0 to 5.6 ± 1.0 l/min). These changes were transient, and the CVP, WPP, and SAP had returned to their baseline levels at the time of clamping of the hepatic pedicle. Following clamping of the hepatic pedicle, there was an increase in SAP, from 91 ± 2 to 118 ± 3 mmHg, a decrease in cardiac outflow, from 5.2 ± 1.3 to 4.3 ± 1.5 l/min, and minimal change in the WPP, from 11.1 ± 3.3 to 11.4 ± 2.8 mmHg. These variations were not significantly different from those observed during open surgery (Fig. 1).

Intraoperative course

No patient was converted, and the procedure was completed within a mean time of 177 ± 57 min (range, 50–270 min). Liver transection was performed with intermittent (n = 6) or continuous (n = 6) clamping of the hepatic pedicle in 12 patients, with a mean duration of 33 ± 12 min. In the remaining 9 patients (including 4 who underwent left lateral segmentectomies), no significant bleeding occurred during liver transection, and the hepatic pedicle was not clamped. The overall mean intraoperative blood loss was 218 ± 173 ml (range, 50–800 ml). The duration of surgery and overall

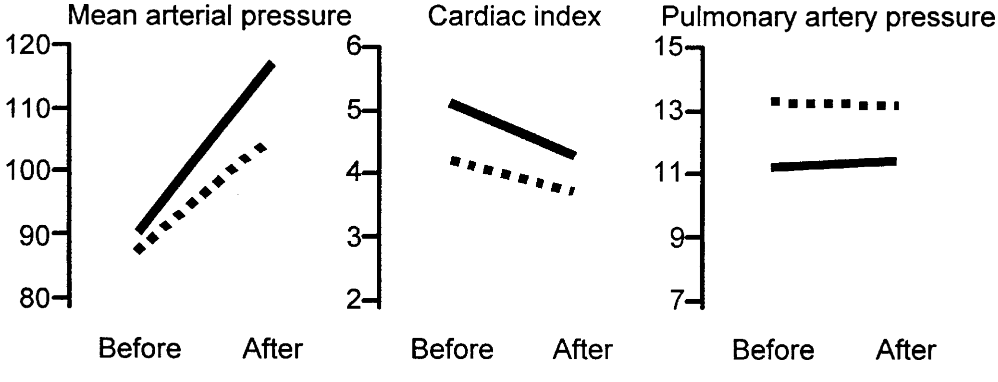

Fig. 1. Mean arterial pressure (mm Hg), cardiac index (l/min), and pulmonary artery pressure (mm Hg) before and 5 min after the clamping of the hepatic pedicle during laparoscopic (*black lines*) or open (*dotted lines*) surgery

Table 2. Intra- and postoperative outcomes in 21 patients undergoing resection of a benign liver tumor by laparoscopy and in 21 patients individually matched for age, sex, body mass index, topography of the tumor, and extent of resection, operated by open surgery

	Laparoscopy (*n* = 21)	Open surgery (*n* = 21)	*P*
Duration of surgery (min)	177 ± 57	156 ± 42	NS
Intraoperative blood loss (ml)	218 ± 173	285 ± 178	NS
Delay to oral intake (days)	1.8 ± 1.0	2.6 ± 0.6	0.008
Cumulative dose of morphine (mg)	15.5 ± 18.3	31.6 ± 19.9	0.02
Cumulative dose of acetaminophen (g)	9.1 ± 5.6	8.7 ± 4.8	NS
Duration of in-hospital stay (days)	5.1 ± 1.3	6.5 ± 1.0	0.0002
Postoperative complications (no. of patients)	2	2	NS

Data values are expressed as mean ± SD unless otherwise stated
NS, Not significant

intraoperative blood loss in patients undergoing laparoscopic and open surgery were comparable (Table 2). A single patient with a steatotic liver who had undergone a bisegmentectomy by laparoscopy required intraoperative transfusion of two units of autologous blood. No patient experienced significant changes in end-tidal CO_2 and O_2 saturation, and in the four patients monitored by transesophageal Doppler ultrasound, no significant passage of gas bubbles through the heart could be demonstrated.

Postoperative course

Postoperative serum transaminase peaked on day 1 (from 20 ± 8 to 101 ± 72 IU/l for aspartate aminotransferase [ASAT]) and had almost normalized on day 3 (Fig. 2). Although mean serum transaminases were significantly lower following laparoscopic surgery on day 3 (ASAT, 47 ± 23 vs 70 ± 34 IU/l; $P < 0.05$), their values were comparable on day 5 to those observed in the control group of patients undergoing open liver surgery. Serum bilirubin and prothrombin time remained within the normal ranges in both groups. Two (10%) patients experienced local complications following laparoscopic surgery. One patient developed a biliary leak following segment 5 resection (despite a negative intraoperative leakage test) that was treated by open surgery through a 5-cm-wide elective subcostal incision on postoperative day 3. Another patient experienced a painful hematoma following resection of segments 5 and 6 that did not require specific treatment. Both patients were discharged on postoperative day 8. There were also two (10%) complications in the control group of patients who underwent open liver surgery, one patient with pleural effusion and one with asymptomatic fluid collection. These two patients were discharged on postoperative days 7 and 8, respectively.

As shown in Table 2, cumulative morphine (but not acetaminophen) consumption was significantly lower

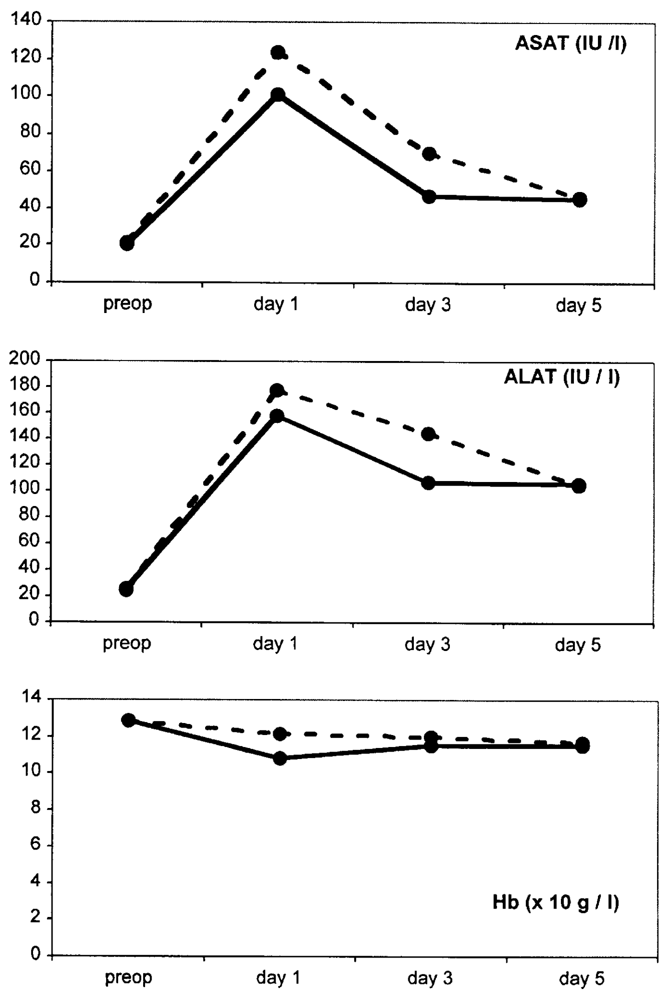

Fig. 2. Kinetics of postoperative Aspartate aminotransferase (*ASAT*), Alanine aminotransferase (*ALAT*), and hemoglobin (*Hb*) levels in patients undergoing liver resection by laparoscopic (*black lines*) or open (*dotted lines*) surgery

following laparoscopic surgery, due to a decreased requirement on postoperative day 1 (10 ± 6 vs 23 ± 12 mg; $P = 0.007$). Delay to oral intake following laparoscopic surgery was significantly lower than that after open surgery. The difference was, however, limited (1.8 vs 2.6 days). Similarly, the duration of in-hospital stay was significantly reduced following laparoscopic surgery. This difference was greater following limited resection (4.3 vs 6.3 days) than after the resection of one or two segments (5.5 vs 6.8 days).

Discussion

The aim of the present study was to report our prospective evaluation of the risks and potential benefits of laparoscopic liver resections in patients with no underlying chronic liver disease undergoing limited resection of benign tumors. The reasons for focusing on benign liver tumors were that the results of minimally invasive surgery should be shown to be equivalent to or better than open surgery prior to justifying its use in the setting of cancer, due to the additional risk of peritoneal seeding and wound recurrence.[18] We have found that: (1) laparoscopic liver resections can be performed using exactly the same technique as that used during open surgery, and, in particular, we have found that clamping of the hepatic pedicle is well tolerated; (2) the risk of intraoperative bleeding and of gas/air embolism is not increased by laparoscopic surgery, and (3) the laparoscopic approach is associated with some advantages compared with open surgery.

Open liver surgery has reached a high level of safety. In patients with no underlying liver disease, the mortality rate has decreased to 1% and the morbidity rate and transfusion requirement have decreased to less than 30%.[19–24] Several technical and technological advances account for this increased safety, all of which aim at preventing intraoperative bleeding. These include the vascular clamping of the hepatic pedicle,[25] the lowering of CVP,[22,26] and the use of the ultrasonic dissector.[27] Our first aim was, therefore, to assess whether these tools could be safely used during a laparoscopic approach.

The ultrasonic dissector has been adapted for laparoscopy so as to allow its introduction through a 10-mm trocar, and it could be used in the same way as during open surgery. The only drawback is that the aspiration device attached to it tends to aspirate the pneumoperitoneum. This, however, was easily overcome with a high-flow insufflator. Alternatively, others have successfully used the harmonic scalpel.[9]

Previous clinical and experimental studies have suggested that the CO_2 pneumoperitoneum was associated with impaired portal blood flow and poor hemodynamic tolerance to the Pringle maneuver.[28–30] We have shown, in contrast, that the hemodynamic variations induced by the pneumoperitoneum were easily reversible, so that by the time that clamping of the hepatic pedicle was required, the parameters studied had returned to the pre-insufflation values. Clamping was associated with an increase in SAP and a decrease in CVP and cardiac outflow, but the magnitudes of these changes were comparable to those observed during open surgery.[16,17] These results indicate that intermittent clamping of the hepatic pedicle, which is the vascular control technique of reference,[17] can be used safely during conventional carbon dioxide pneumoperitoneum laparoscopy, and that the hemodynamic monitoring using this technique should not be different from that used during open surgery.

Another theoretical drawback of the pneumoperitoneum technique is the potential risk of gas embolism.[31] In the current and previous[10] series where this risk was carefully monitored no gas embolism was observed. These results confirm that there is persistent blood flow in abdominal veins to the inferior vena cava with no retrograde venous penetration of carbon dioxide bubbles, provided that the intraabdominal pressure is less than 20 mmHg.[32]

Altogether, these results suggest that there is no rationale for preferring a gasless laparoscopy, which is usually associated with reduced surgical exposure.[33–35]

The amount of intraoperative blood loss during laparoscopic and open surgery was comparable. With increasing experience, we have found that clamping of the hepatic pedicle did not always prove necessary during laparoscopic hepatectomies due to the tamponading by the pneumoperitoneum.[36] This, however, may preclude accurate intraoperative recognition of blood or biliary leak from the cut surface, which resulted in local complications in two of our patients. Although these complications may also occur after open surgery, they probably should deserve special consideration during laparoscopic liver resection. Our current policy is to check the cut surface at low insufflation pressure after a 15-min period of complete desufflation, and to perform routine abdominal ultrasound on postoperative day 4 or 5.

Despite a slightly longer operating time, the benefit of the laparoscopic approach over open surgery was a quicker improvement in serum transaminase levels, a reduced postoperative analgesic requirement, a shorter delay to oral intake, and a reduced hospital stay. Many noncomparative studies have claimed that these advantages in favor of the laparoscopic approach were obvious in patients undergoing cyst resection or tumorectomies.[6,8,9] Our comparative study suggests that they are, in fact, somewhat limited in patients undergoing segmentectomies or bisegmentectomies. Serum transaminase was lower on day 3 but had normalized on day 5 with both techniques. The reduced analgesic intake was obvious only on day 1 to achieve the same control of pain, and the duration of the in-hospital stay was reduced by only 1 day. Hence, these benefits of the laparoscopic approach appear to be much less obvious after liver resections of up to two segments than after nephrectomies,[37] adrenalectomies,[38] splenectomies,[39] or colorectal surgery.[40,41]

In conclusion, we have found that laparoscopic resections were safe when performed by surgeons with a dual expertise in both laparoscopic and open liver surgery. We do not, however, believe that laparoscopy will become established as the standard approach for patients requiring segmentectomies or bisegmentectomies. As a matter of fact, the proportion of benign liver tumors requiring resection has become very low and, retrospectively, the great majority of our patients with focal nodular hyperplasia or angioma should not have been operated. As for malignancies, the indication for a laparoscopic liver resection with a curative intent is not established yet, in terms of balancing its limited intra- and early postoperative advantage over open surgery with the potential hazard of tumor dissemination and inadequate margins.[10] Its main indication is probably the subgroup of patients requiring wedge resections of superficially located tumors.[5] Other patients should still undergo open surgery, unless prospective trials demonstrate the feasibility of major resections with the laparoscopic approach, or a clearer superiority of the laparoscopic approach.

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