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Laparoscopic Partial Hepatectomy in the Rat: A New Resectional Technique

Key Words
Liver resection
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CO_2 pneumoperitoneum
Gasless laparoscopy

Abstract
Background: Rats are widely used for basic research in laparoscopic surgery. We have developed a new technique of laparoscopic partial hepatectomy in the rat. **Methods:** 40 American Cancer Institute rats were randomized into 3 groups. Group A (n = 14) underwent laparoscopic liver resection using a CO_2 pneumoperitoneum. Group B (n = 14) was operated on with a gasless laparoscopic technique using a lifting device. A control group C (n = 12) underwent conventional open liver resection. In each group half of the animals underwent single lobectomy and the other half bilobectomy. **Results:** The liver resection was performed successfully in all 40 rats. No conversion to open surgery was necessary. No mortality or morbidity was observed. **Conclusions:** This new technique of laparoscopic partial hepatectomy proved to be feasible and safe. It is the first description of a laparoscopic hepatic resection in the rat that could prove valuable in further investigations of liver physiology and pathology.

Introduction

The rat is widely used as a small animal model for basic research of open [1] and laparoscopic surgery [2]. In 1931 the first resectional techniques for liver surgery in the rat were reported by Higgins and Anderson [3] who resected up to 70% of the liver parenchyma. Investigations in laparoscopic research have mainly focused on adhesion formation [4], stress hormones and cytokine reactions [5], cardiorespiratory effects of the CO_2 pneumoperitoneum [6], and the severity of peritonitis in perforated gastric ulcer [7] as well as on tumor growth and tumor cell spread [8–12]. Such studies have been conducted using laparoscopic Nissen fundoplication [2], laparoscopic colon surgery [13], laparoscopic nephrectomy and splenectomy [14].

Until now, no series of laparoscopic liver resections has been reported in the rat. Therefore, the aim of the present study was to investigate the feasibility of laparoscopic partial hepatectomy in the rat.

Materials and Methods

Animals
The experiments were approved by the Animal Ethics Committee of the State of Berne and performed according to international guidelines.

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Fig. 1. Small animal operating table and rat with installed pneumoperitoneum.

Forty male American Cancer Institute rats (Harlan CPB, 3700 Zeist, The Netherlands) weighing 250–300 g were used. The animals were kept in free-standing cages, acclimatized to normal laboratory conditions and fed a standard rat pellet diet with tap water ad libitum. On the day of surgery only water was allowed.

Study Design

The animals were randomized into 3 groups: group A (n = 14) underwent laparoscopic liver resection with a CO_2 pneumoperitoneum, and group B (n = 14) gasless laparoscopic liver resection using a special lifting device to create an intra-abdominal working space. In group C (n = 12), which served as a control group, open liver resection by conventional open laparotomy was performed. In each group, half of the animals underwent either single lobectomy or bilobectomy. The animals were killed 2 weeks postoperatively after which autopsy was conducted.

Surgical Procedures

All groups were anesthetized by intraperitoneal injection of a mixture (1 ml volume/kg body weight) of 25 ml 5% glucose, 5 ml Sedalin®, 5 ml Xylapan® and 10 ml Narketan®. The animals were shaved and placed on a small animal operating table (Karl Kaps, 35614 Asslar, Germany) and secured in a supine position.

Group A

Laparoscopic Liver Resection with a CO_2 Pneumoperitoneum. A 5-mm-long skin incision was made in the abdomen midway between the xiphoid process and the pubic area. The camera trocar with an insufflation side port was introduced into the peritoneal cavity under direct visual control. A purse string suture was applied to prevent gas leakage. The laparoscope was attached to a flexible arm. This setup allowed the surgeon, sitting at the foot of the operating table, to use a two-handed operation technique while facing the monitor [2]. All the laparoscopic instruments were 2.7 mm in diameter, and scissors, straight and angled forceps and needle holders were used (Wolf®, Knittlingen, Germany). Small-sized surgical instruments for hand surgery were used for all open procedures. No electric coagulation device was needed. The CO_2 pneumoperitoneum was installed with a maximum intra-abdominal pressure of 4 mm Hg (fig. 1). Following a diagnostic overview of the abdominal cavity, two additional working trocars were introduced into the upper right and left hemiabdomen under direct vision.

Technique of Lobectomy. The left lateral hepatic lobe was identified for resection. For better exposure, the median lobe was displaced cranially. In order to perform a lobectomy of the left lateral lobe, division of the pars flaccida of the lesser omentum was necessary. A pretied loop ligature (Endoloop®, 3.0 plain catgut, Johnson and Johnson, Spreitenbach, Switzerland) was then placed around the base of the left lateral liver lobe under endoscopic guidance without any further mobilization of the liver. The ligature was tied firmly. Resection was performed with scissors about 3–5 mm distal to the ligature, leaving only a small stump of liver tissue. This stump prevented the knot from slipping (fig. 2a, b).

Technique of Bilobectomy. For bilobectomy, division of the falciform ligament as well as the pars flaccida of the lesser omentum was performed. The left lateral lobe and the left part of the median lobe were identified for resection. A pretied loop ligature (Endoloop®) was slipped through the umbilical fissure of the median lobe and placed at the base of the common pedicle. The ligature was tied and parenchymal resection performed leaving an adequate stump of the liver remnant (fig. 2c).

Extraction of the resected liver lobe was achieved by distally extending the camera trocar site a few millimeters.

Group B

Gasless Laparoscopic Liver Resection using a Lifting Device. Two subcutaneous sutures were firmly placed subcutaneously in the upper left and right abdominal wall. They were attached to a lifting device to create tension in the upper surface of the abdominal wall. This created a sufficiently wide intra-abdominal working space to perform

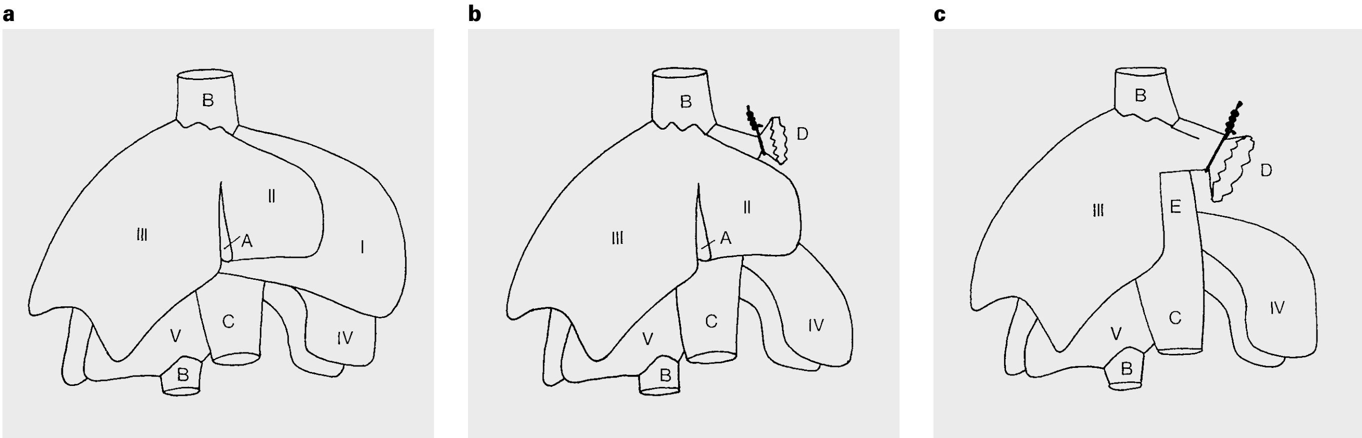

Fig. 2. I = Left lateral lobe; II = left part of median lobe; III = right part of median lobe; IV = caudate lobe; V = right lateral lobe; A = umbilical fissure; B = vena cava; C = liver hilum/lesser omentum; D = resection stump; E = pericaval parenchymatous axis. **a** Liver anatomy. **b** Situation after lobectomy: left lateral lobe removed. **c** Situation after bilobectomy: left lateral lobe and left part of the median lobe removed.

Fig. 3. Lifting device for gasless laparoscopic surgery.

hepatic resection (fig. 3). The operative laparoscopic procedure for partial liver resection was the same as described for group A.

Group C

Conventional Open Liver Resection. Conventional open liver resection was performed as described by Higgins and Anderson [3]. A 3-cm-long midline laparotomy was performed. The xiphoid process was mobilized and the falciform ligament, as well as the pars flaccida of the lesser omentum, was divided. After externalization of the left lateral lobe, resection was performed by placing a ligature (3.0 PDS®, Johnson and Johnson, Spreitenbach, Switzerland) around the base of the left lateral liver lobe. Bilobectomy was performed by including the left part of the median lobe in the ligature and performing resection of both lobes. The laparotomy was closed with a two-layer technique and a running suture.

Immediately after surgery, the animals were placed in their cages and all had free access to water and rat chow.

Statistical Analysis

Data are expressed as mean ± SD or percent. Means were compared using the unpaired t test. A $p < 0.05$ was considered to be statistically significant.

Results

The mean operative time in all 3 groups was 22 ± 2 min. Intraoperative hemostasis was easily achieved at all resection margins by applying a pretied 3.0 Endoloop® ligature for the laparoscopic groups or a 3.0 PDS® ligature in the open group. No conversion to the open technique was necessary. Blood loss during the intervention was minimal and unmeasurable. No intra- or perioperative mortality or morbidity (bleeding, biliary leakage, infection) was observed. All animals had a normal proportional postoperative weight gain, regardless of whether one or two lobes had been resected. The postmortem investigation performed 2 weeks postoperatively showed no wound infections, no intra-abdominal abscess formation and no sign of former bleeding at the resection margins. There was no sign of bile leakage encountered in the abdominal cavity or on the resection surface of the liver. Granuloma formation was frequently found at the resection margins around the catgut ligature in group A (10/14 animals, 71%) and group B (9/14 animals, 64%). Although there was no statistically significant difference between groups A and B, it was a rare event in group C (2/12 animals, 17%) where a PDS® ligature was applied. Comparison of group C with either group A or B was statistically significant ($p < 0.05$).

Discussion

The rat is a universally established important small animal model in basic research into open and laparoscopic surgical procedures [1–4, 8, 13, 14]. It offers the advantages of being a well-studied laboratory animal with an abundance of internationally reported research results. Furthermore, it is inexpensive to breed, buy and house. The rat is therefore well suited to basic laparoscopic investigations. Since one of our main scientific interests is hepatic resectional procedures, we sought to study the feasibility of partial hepatectomy in the rat. The first series of open hepatic resections in the rat was published by Higgins and Anderson [3] in 1931, in which they applied a coarse linen ligature around the common base of the large median lobe and the left lateral lobe of the liver. Resection followed leaving an adequate stump. With this technique, they were able to resect 65–75% of the liver parenchyma. Their technique has since been widely used in various experimental settings with hardly any modifications. We have now tried to combine liver resections in the rat with the new technique of laparoscopic surgery. We chose to perform lobectomy (left lateral lobe) and bilobectomy (left lateral lobe and the left part of the median lobe). We deliberately did not perform a classic bilobectomy of the liver (65–75% of the liver parenchyma), as described by Higgins and Anderson [3], in order not to compromise animal survival.

To our knowledge, this is the first report of laparoscopic liver resection in the rat, although it is already widely used as a valuable animal model for basic laparoscopic research. On the one hand, research has focused on the pathophysiological effects of laparoscopy and pneumoperitoneum on cardiovascular function [6], stress hormone and cytokine reaction [5] and adhesion formation [4]. While on the other hand, new laparoscopic surgical procedures have been investigated such as laparoscopic Nissen fundoplication [2], laparoscopic colon surgery [13], laparoscopic splenectomy and nephrectomy [14].

Our study showed that laparoscopic partial liver resection is feasible, safe and reproducible. The application of a pretied ligature to the base of the liver lobe with subsequent resection of the liver parenchyma proved to be a simple and effective method. It allowed safe hemostasis. Furthermore, we had the impression that because of the positive intra-abdominal pressure during CO_2 laparoscopy, the tendency to bleed was less compared to open or gasless surgery. The blood loss, however, was minimal and could not be measured, which prevented scientific evaluation of this observation.

Gasless laparoscopic partial hepatectomy proved to be technically more difficult than CO_2 pneumoperitoneum. This was mainly due to the reduced triangular working space and the decreased visibility during resection due to the increased capillary bleeding in the absence of a positive intra-abdominal pressure.

There was no mortality or morbidity in any of the 3 groups. The only major difference found between the open and the laparoscopic groups was granuloma formation at the hepatic resection margins. This difference could be due to an excessive inflammatory response to the 3.0 plain catgut Endoloop® ligature, which was used in the laparoscopic groups because of its lower price. A significantly lower percentage of granuloma formation was noticed in the group of open partial hepatectomy where a 3.0 PDS® ligature was applied.

No technical problems were encountered when the procedures were performed by skilled laparoscopic surgeons. These results are encouraging.

There are several conceivable applications of this new technique for laparoscopic partial hepatectomy in the rat. One is its use in basic research into laparoscopic tumor surgery. A second application may be in the field of liver pathophysiology and liver regeneration. Numerous cirrhotic rat models have been described. The laparoscopic technique of partial liver resection could be used to obtain surgical biopsies for histological and biochemical analysis. This minimally invasive technique avoids laparotomy and therefore may reduce morbidity and mortality in artificially diseased, fragile, cirrhotic laboratory rats.

In conclusion, laparoscopic partial hepatectomy (lobectomy or bilobectomy) in the rat is feasible and safe. It may represent a valuable tool for further basic research into laparoscopic surgery as well as for other investigations of liver physiology and pathology.

Acknowledgment

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References

1 Castaing D, Houssin D, Bismuth H (eds): Hepatic and Portal Surgery in the Rat. Paris, Masson, 1980.
2 Berguer R, Gutt C, Stiegmann GV: Laparoscopic surgery in the rat. Description of a new technique. Surg Endosc 1993;7:345–347.
3 Higgins GM, Anderson RM: Experimental pathology of the liver. I. Restoration of the liver of the white rat following partial surgical removal. Arch Pathol 1931;12:186–202.
4 Krähenbühl L, Schäfer M, Kuzinkovas V, Renzulli P, Baer HU, Büchler MW: An experimental study of adhesion formation in open and laparoscopic fundoplication. Br J Surg 1998, in press.
5 Trokel MJ, Bessler M, Treat MR, Whelan RL, Nowygrod R: Preservation of immune response after laparoscopy. Surg Endosc 1994;8: 1385–1388.
6 Dalton M, Hildreth J, Matsuoka T, Berguer R: Determination of cardiorespiratory function and the optimum anesthetic regimen during laparoscopic surgery in the rat model. Surg Endosc 1996;10:297–300.
7 Bloechle C, Emmermann A, Treu H, Achilles E, Mack D, Zornig C, Broelsch CE: Effect of a pneumoperitoneum on the extent and severity of peritonitis induced by gastric ulcer perforation in the rat. Surg Endosc 1995;9:898–901.
8 Bouvy ND, Marquet RL, Hamming JF, Jeekel J, Bonjer HJ: Laparoscopic surgery in the rat. Beneficial effect on body weight and tumor take. Surg Endosc 1996;10:490–494.
9 Bouvy ND, Marquet RL, Jeekel H, Bonjer HJ: Impact of gas(less) laparoscopy and laparotomy on peritoneal tumor growth and abdominal wall metastasis. Ann Surg 1996;224:694–700.
10 Jacobi CA, Sabat R, Bohm B, Zieren HU, Volk HD, Müller JM: Pneumoperitoneum with carbon dioxide stimulates growth of malignant cells. Surgery 1997;121:72–78.
11 Mathew G, Watson DI, Rofe AM, Baigrie CF, Ellis T, Jamieson GG: Wound metastasis following laparoscopic and open surgery for abdominal cancer in a rat model. Br J Surg 1996; 83:1087–1090.
12 Watson DI, Mathew G, Ellis T, Baigrie CF, Rofe AM, Jamieson GG: Gasless laparoscopy may reduce the risk of port-site metastasis following laparoscopic tumor surgery. Arch Surg 1997;132:166–168.
13 Berguer R, Gutt CN: Laparoscopic colon surgery in a rat model. A preliminary report. Surg Endosc 1994;8:1195–1197.
14 Giuffrida MC, Marquet RL, Kazemier G, Wittich P, Bouvy ND, Bruining HA, Bonjer HJ: Laparoscopic splenectomy and nephrectomy in a rat model. Description of a new technique. Surg Endosc 1997;11:491–494.