



Laparoscopic Resection for the Treatment of Liver Tumors

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Abstract

Open hepatectomy remains the fundamental and one of the most common surgical techniques for the treatment of primary and secondary liver tumors, but Laparoscopic Liver Resection (LLR) is now gaining more and more importance.

The aim of the study was to evaluate the efficacy and safety of laparoscopic resection of liver tumors based on the clinical experience of the authors.

LLR was performed in 53 patients (26 women and 27 men). The most common indication for the laparoscopic resection of liver tumors was metastatic colon cancer. We performed 19 non-anatomical (wedge) resections, 11 segmentectomies, 10 anatomical resections, 8 hemihepatectomies, 3 radicalizations due to gallbladder cancer, and 2 liver cyst fenestrations. Simultaneous procedures were performed in 5 cases.

The mean operating time for the laparoscopic resection of liver tumors was 307 min. The mean intraoperative blood loss was 270 ml. Complications were reported in 10% of cases. The mean hospitalization time was 7 days.

Slightly longer operating time and greater blood loss were found in patients treated with LLR compared to those who had open surgery. Recovery time was shorter in patients who had laparoscopic surgery. Early results of cancer treatment were comparable to those for open surgeries. LLR was associated with lower rates of postoperative complications.

Laparoscopic liver resections reduce intraoperative trauma and the number of postoperative complications, and shorten the hospitalization time and recovery. These procedures are safe in cancer patients. A particular advantage of laparoscopic surgery is observed in patients with cirrhosis, the elderly, and patients with coexisting internal diseases.

Keywords: Liver tumors; Laparoscopic resection; LLR

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Introduction

Open liver resection remains the fundamental and one of the most common surgical techniques for the treatment of primary and secondary liver tumors. Outcomes of surgical treatment for liver tumors have been systematically improving in recent years due to advances in surgical techniques and better understanding of liver anatomy. Reportedly, a breakthrough in the treatment of liver tumors is expected with the introduction of new minimally invasive techniques, including laparoscopy.

A growing number of publications indicate that laparoscopic resection of liver tumors is slowly replacing the most common open liver surgery. Many researchers have demonstrated that laparoscopy is safe and well tolerated by the patient, and offers outcomes in the treatment of cancer comparable to classical open procedures [1]. The first reports on laparoscopic liver resections date back to the early 1990s. They indicated LLR as an alternative to open surgery, allowing a reduction in intraoperative trauma and shortening the recovery time [2,3]. Laparoscopic liver surgery has been developing dynamically, and in 2008 the efficacy and safety of this technique was confirmed during the first international conference on the use of laparoscopy in liver surgery. Recommendations for laparoscopic liver surgery were also established during that conference [4]. Laparoscopy was adopted as a standard procedure for minor resections of the liver during the Second International Consensus Conference on Laparoscopic Liver Resection in 2014. Moreover, it was agreed that further, larger studies are required to establish recommendations for more extensive resections [5]. Advances in surgical instruments and the improved safety of laparoscopic procedures systematically broaden the range of indications for the use of this technique. The exponential growth in the number of

laparoscopic liver resections performed worldwide has been observed in the last two decades [6]. Globally, about 65% of laparoscopic liver resections are performed due to primary and secondary liver cancers, and the other 35% are surgeries for benign tumors [7]. About 30% of patients with hepatocellular carcinoma undergo laparoscopic liver resection [8]. In patients with metastatic colon cancer, medical centers with extensive experience perform about 70% of resections with minimally invasive techniques [9]. Laparoscopic surgery is used less frequently in patients with gallbladder cancer because in many cases the surgery has to be extended to remove and reconstruct the biliary ducts and hilar vasculature of the liver. Nevertheless, good outcomes have been achieved using laparoscopic procedures in the early stages of this type of cancer [10]. Laparoscopic resection can also be used with success to treat other malignant liver tumors, but the number of relevant reports is still limited. The indications for the laparoscopic resection of benign liver tumors are similar to those in open surgery, the most common being giant liver cysts, large hemangiomas and hepatic adenomas.

According to numerous publications, laparoscopic liver resection reduces surgical trauma, intraoperative blood loss, and postoperative pain severity. This procedure also improves the outcome of surgical treatment, especially in patients with cirrhosis and/or other liver disorders [11]. In addition, laparoscopy prevents the formation of postoperative adhesions, which makes any subsequent procedures easier to perform if necessary. Studies demonstrated that long-term outcome measures of cancer treatment such as DFS (Disease-Free Survival) and OS (overall survival) are comparable to those achieved in patients who had open surgery, and one report even documented better overall survival in cirrhotic patients who had laparoscopic procedure (OS 69% vs. 57%) [12]. The use of laparoscopic resection of tumors in patients with chronic liver disease helps reduce the number of intra- and postoperative complications, including intraoperative blood loss, and significantly shortens the recovery time after surgery [13,14]. It is also very important in elderly patients who, due to their age and frequent comorbidities, are a special risk group for open procedures.

Despite the spectacular results of the use of laparoscopy in liver surgery, numerous scientific reports on this subject often ignore the problems that arise when starting this type of procedure. This article presents our clinical experience with laparoscopic liver resection, analysis of data on early results of cancer treatment, and difficulties encountered during surgery.

In Poland there are no precise statistics on the use of laparoscopy for liver resections. Reports presented at conferences show that the number of LLRs performed in Poland is gradually increasing. However, medical databases contain a limited number of publications presenting the experience of clinicians in laparoscopic liver resections [15].

Patients and Methods

Classification of patients

All patients qualified for the laparoscopic resection of liver tumors expressed their consent for this type of treatment. The choice of therapy and qualification of patients were consistent with recommendations established during ICCLLR held in 2014 [5].

For the surgical procedure we qualified patients with metastases who had already had the primary tumor removed (at least one month before LLR), or patients with primary lesions in the liver or bile ducts.

A few patients with synchronous metastases from colon cancer (max. 3 cm in diameter) in the subcapsular area of the anterior and left segments of the liver were qualified for the simultaneous resection of the primary focal lesion and liver tumor. Tumors were located in all segments of the liver (I to VIII).

Technique of laparoscopic resection

During laparoscopic liver resection the patient was placed in a reverse Trendelenburg position with legs open wide. In most cases 4 to 5 trocars were used to perform the procedure. Trocars were usually inserted beneath the right costal arch. A camera was inserted and the advancement of cancer inside the abdominal cavity was assessed. In the next stage, laparoscopic ultrasound of the liver was performed with a special probe to determine the size of the tumor, and its position in relation to the hepatic vessels, and the resection margin. Depending on the planned type of resection, a necessary part of the liver was released from the ligaments using electro-surgical instruments. If right hemihepatectomy was to be performed, short hepatic veins were sealed and cut, the venous ligament was dissected to create access to the right hepatic vein. The right hepatic vein was occluded before or after dissecting liver parenchyma, depending on the intraoperative situation. During left hemihepatectomy the medial/left hepatic veins were usually occluded after dissecting the liver parenchyma. Cholecystectomy was performed depending on the extent of the planned resection and the presence of gallstones. During each resection the hepatoduodenal ligament was always prepared for the Pringle manoeuvre, by tying a tape around the ligament and the placement of tape ends outside *via* a drain tube. There are different options for the dissection of hepatic lobar vessels during hemihepatectomy: The whole Glissonean pedicle can be detached from the liver lobe extrafascially (extraglissonian approach), or each vessel may be detached separately (intraglissonian approach). Extrafascial dissection of Glissonean pedicle with vascular stapler shortens the operating time, but it is not always feasible during laparoscopy. Separate detachment of each hilar element is more time consuming, but allows for better identification of the anatomy of the vessels and bile ducts. The parenchyma was usually separated using a CUSA, while the clamp-crush technique was used less often. Smaller vessels during liver resection were sealed with an ultrasonic knife, and larger ones with metal or plastic clips. Cooperation with the anesthesiological team was vital to reduce the supply of fluids and maintain a low CVP at the stage of cutting the parenchyma and the separation of the IVC. This allowed for a significant reduction in intraoperative blood loss. Insufflation of the abdomen during laparoscopy produces an additional hemostatic effect, and for that purpose the intra-abdominal pressure was increased to 16 mmHg during the dissection of the parenchyma. In our medical center the following strategy was adopted to reduce intraoperative blood loss: When blood loss is greater than 300 ml and there is still more than 50% of the parenchyma to dissect, we convert to open surgery. Usually, the tumor was removed through minilaparotomy beneath the right costal arch; in the case of postoperative complications and indications for laparotomy, incisions used for the placement of trocars and the minilaparotomy may be connected into one. After the removal of the tumor the patient was checked for hemostasis and potential bile leakage. A drain tube was placed in most cases, and then usually removed on day 2 or 3 after surgery.

Aim of the study

The aim of the study was to evaluate the efficacy and safety of laparoscopic resection of liver tumors. We assessed operating

Table 1: Characteristics of patients.

Number of patients	53
Women/men, n (%)	26/27 (49%/51%)
Mean age (range)	67 (45-92)
Child-Pugh score	A-53 (100%)
Primary diagnosis, n (%)	
MTS colon cancer	36 (68%)
MTS ovarian cancer	3 (5.6%)
Gallbladder cancer	3 (5.6%)
CCC	1 (1.8%)
MTS lung cancer	2 (3.6%)
MTS malignant neoplasm of corpus uteri	1 (1.8%)
MTS breast cancer	1 (1.8%)
HCC	1 (1.8%)
FNH	3 (5.6%)
Simple hepatic cyst	2 (3.6%)

MTS: Metastasis; CCC: Cholangiocarcinoma; HCC: Hepatocellular Carcinoma; FNH: Focal Nodular Hyperplasia

time, intraoperative blood loss, postoperative hospitalization time, potential complications, and early results of liver resection using the presented techniques in cancer patients.

Results

Laparoscopic liver resection was performed in 53 patients (26 women and 27 men). The mean age of patients was 67 years. All patients had a good performance status corresponding to ECOG grades 0 to 1, without clinical or laboratory evidence of liver failure. The most common indication for the laparoscopic resection of liver tumors was metastasis from colon cancer (Table 1).

Conversion to laparotomy was necessary in 3 cases: in 2 patients because of intraoperative bleeding and in one patient for oncological reasons (suspected inadequate margin of resection). The extent of resection was different from wedge resections to right or left hemihepatectomy, depending on the number, location and size of the tumor, and the patient's status. We performed 5 surgeries combining the resection of a bigger liver tumor and radiofrequency ablation of a smaller one. Simultaneous resection of a primary tumor and metastatic tumor of the liver was performed in 5 patients with colon cancer (Table 2).

Qualification of patients and indications for laparoscopic liver resection are similar to those for open surgeries. Particular attention should be paid to patients with a history of surgical procedures on the organs of the upper abdomen, due to the risk of postoperative adhesions after previous procedures, and to patients with heart and/or lung diseases that may cause poor tolerance of insufflation. Difficulties in the laparoscopic technique are caused by large tumors (>0 cm), parahilar tumor location, and infiltrates or thrombi in the lobar vessels of the liver. Tumors that infiltrate the diaphragm and retroperitoneal adipose tissue are not contraindications for the use of laparoscopy.

The mean operating time for the laparoscopic resection of liver tumors was 307 min. The operating time was longest for laparoscopic hemihepatectomy (mean 420 min), and left hemihepatectomy was on average 1 h shorter than right hemihepatectomy. The mean operating time for laparoscopic right posterior bisegmentectomy was 300 min

Table 2: Types of surgery.

Type of surgery	Number of procedures	Mean blood loss, ml
Non-anatomical resection:	19	
Anterior segments + segment IV	9 + 3 (simultaneous procedure*)	150
Posterior segments	4	150
Left lateral	1 (simultaneous procedure*)	338
More than one resection during one procedure	2	350
Hepatic segmentectomy:	11	
Left lateral segments	2	350
Segment IVA, B	3	175
Right anterior segments	3	370
Right posterior segments	2	500
segment I	1	350
Bisegmentectomy, left lateral	3+1 (simultaneous procedure*)	100
Bisegmentectomy, right posterior	6	700
Hemihepatectomy, left	5	270
Hemihepatectomy, right	3	350
Radicalization due to gallbladder cancer with lymphadenectomy	3	230
Liver cyst fenestration	2	50
Total:	53	

*simultaneous procedure - colon resection due to cancer combined with resection of metastasis from the liver during one procedure

and it was the longest procedure compared to other anatomical resections of one or two segments of the liver. The mean operating time for left lateral bisegmentectomy was 180 min. The operating time for wedge liver resection differed depending on tumor location and was from 120 min for tumors in anterior segments of the liver to 300 min when tumors were located in posterior segments. Laparoscopic surgeries were longer than open surgeries, but a gradual reduction in the operating time was achieved.

The mean intraoperative blood loss in patients who had laparoscopic procedures was 270 ml. Blood loss was lowest during left lateral bisegmentectomy (mean 100 ml) and wedge liver resection (mean 150 ml). The mean blood loss associated with segmentectomy was 270 ml and was higher in patients with tumors located in posterior segments of the liver. The mean blood loss during hemihepatectomy was 325 ml and was higher during the resection of the right lobe. Blood loss was highest during right posterior bisegmentectomy (700 ml). In 13 patients during laparoscopic liver resection, we did not use the Pringle manoeuvre (liver cyst fenestration and hemihepatectomy were not considered). Most of these surgeries were wedge liver resections (12) and one surgery was performed to remove the left lateral segments of the liver. During hemihepatectomy, we tried to avoid the Pringle manoeuvre and limit the occlusion of the lobar vessels. The Pringle manoeuvre was used during other resections.

The analysis of operating time for all laparoscopic anatomical liver resections and the intraoperative blood loss revealed that procedures for the posterior segments of the liver were longer and associated with a risk of greater blood loss. Because of the need to separate the right lobe of the liver and difficult access to lesions located in segments VI and VII, these procedures should be regarded as more complicated in technical terms. At the beginning of this procedure a team of two surgeons may encounter difficulties when manipulating the right lobe

of the liver and achieving the necessary traction during the surgical separation of the parenchyma. The hand-assisted technique may be used to solve these problems during procedures on the posterior segments of the liver. In this technique the operator places the left hand inside the incision under the right costal arch, which is later used to remove the tumor through a special sleeve, and pulls the posterior segments of the liver. This manoeuvre helps to manipulate the right lobe of the liver. The same technique can be used in patients with large tumors located in the right lobe of the liver.

The use of laparoscopy for the resection of focal liver lesions is associated with faster recovery of patients after surgery. Our patients treated with this technique were able to eat, get out of bed and walk as early as on the first postoperative day. Shorter postoperative rehabilitation was also observed. Moreover, pain severity was much lower compared to patients after resections using the open technique. This helped reduce the use of opioid analgesics in the postoperative period. The number of postoperative complications in patients after laparoscopic liver resection was lower compared to patients treated with open surgery. All these aspects reduced hospital stay time by about 1.5 days on average compared to patients who had liver resection using the classical technique. The mean hospital stay after laparoscopic liver resection was 7 days.

Complications were reported in 5 patients (10%). One patient (with a history of peritonitis) had a perforation of the small intestine undetected during the separation of adhesions and was treated surgically. When operating on this patient, we found numerous adhesions near the left lobe of the liver, where the metastatic tumor was located. The second patient had a perforation of the common bile duct (Bismuth type 1 injury) following lymphadenectomy of the hepatoduodenal ligament and was treated surgically by the placement of a Kehr's tube. Another 3 patients had postoperative biliary leak and were treated by conservative methods with a good outcome. The rate of postoperative complications following laparoscopic liver resections was slightly lower compared to open procedures (10% vs. 12.5%) performed in our hospital department.

Early results of cancer treatment were assessed based on the relapse of cancer within 3 months following liver resection. In this analysis we did not consider 5 patients with benign liver tumors. There were 38 patients with a 3-month-long disease-free survival after laparoscopic liver resection. Cancer relapse in the liver was detected in one patient. Another 9 patients had metastases to other organs. Given the complexity of cancer treatment, it is impossible to assess separately the effect of laparoscopic liver resection on the results of cancer treatment.

Discussion

Laparoscopic liver resection is a procedure that requires knowledge of liver surgery and laparoscopic techniques from the surgical team. According to reported data, the learning curve for wedge laparoscopic liver resections (removal of one or two segments of the liver) requires participation in about 20 to 25 surgeries, and increases to 45-60 for anatomical procedures [16,17]. Difficulties associated with liver resection cannot be evaluated solely by the number of segments removed, because the location of segments is also important. Surgeries to remove tumors in the posterosuperior liver segments are regarded as more complicated. The learning curve for these procedures according to some authors was estimated at 40 surgeries for minor liver resections, and 60 for major procedures [18].

Another study demonstrated that learning from surgeons experienced in liver resection reduces learning time by more than 2 times [19]. These data indicate the role of surgical experience in this type of procedure. In our medical center we initially performed laparoscopic resections to remove small tumors located near the liver capsule (i.e. wedge liver resections). This enabled us to develop an optimal strategy for laparoscopic separation of the liver parenchyma and for laparoscopic Pringle manoeuvre performing. As we gained more experience, we gradually extended the scope of these procedures. It is worth noting that our surgical team has participated in numerous courses on laparoscopic liver surgery in Poland and abroad.

The use of modern instruments for the separation of the hepatic parenchyma, such as the water-jet or CUSA (cavitron ultrasonic surgical aspirator) during LLR helps to save vascular structures and minimize intraoperative blood loss. Moreover, it increases the comfort of operators and improves the precision in the sealing of vessels and bile ducts. The advantage of these instruments is to obtain an additional resection margin. The easiest and most affordable way to separate the hepatic parenchyma is the clamp-crush technique, which involves the separation of the parenchyma using forceps and selective occlusion of vascular structures. It is quite an old technique but still highly rated for its effectiveness [20]. Considering the large number of relevant reports, it can be concluded that the effectiveness of the parenchymal separation technique largely depends on the experience and preferences of the surgical team and the results are comparable [21]. In our opinion, the use of CUSA and periodic occlusion of the hepatoduodenal ligament can significantly reduce intraoperative blood loss and help visualize vascular structures of the liver more precisely, which is particularly important during anatomical resections. The disadvantage of using the CUSA system is that it easily makes laparoscopic optics dirty. Our experience shows that the use of CUSA in patients with advanced fatty liver disease or cirrhosis may lead to injury to the parenchymal vasculature during dissection, and bleeding. In such cases we tend to use the clamp-crush technique combined with bipolar coagulation. There is no consensus on electro-surgical instruments used for laparoscopic liver resection. One of the largest studies comparing different energy devices did not demonstrate the superiority of any of them. Reportedly, the crucial thing during the separation of the hepatic parenchyma is the precise dissection and sealing of hepatic blood vessels, while the type of electro-instrument is of secondary importance [22]. One aspect important from the technical point of view is the temporary occlusion of the hepatoduodenal ligament (Pringle manoeuvre) to reduce blood supply to the liver. Despite advances in techniques for the precise laparoscopic dissection of the liver parenchyma, a number of reports have indicated that the use of the Pringle manoeuvre has a positive effect on the results of treatment in terms of minimized blood loss [23,24]. There are several variants of this manoeuvre during laparoscopy, but none of them has a particular proven advantage. When treating our patients, we occluded the hepatoduodenal ligament on the outside, enabling quick clamping and releasing of the ligament if necessary, and this is especially important during resection. In most procedures we are prepared for the Pringle manoeuvre, and even if we do not plan to use it, we are able to quickly control sudden intraoperative bleeding.

Qualification of patients and indications for laparoscopic liver resection are similar to those in open surgeries. In 2017, data on 2,238 patients from 4 European liver surgery centers were analyzed. The study demonstrated an increase in the number of laparoscopic

procedures performed annually from 5% in 2000 to 43% in 2015. Currently, about 65% of laparoscopic liver resections worldwide are done for malignancy, and the rest are benign tumor resections [6]. Globally, almost 50% of laparoscopic liver resections are because of HCC [25]. In our patients the most common indication for laparoscopic resection of liver tumors was metastatic colon cancer. This is consistent with indications reported a few years ago by Koffron et al. [26]. A study presented by Cherqui revealed that 25% of laparoscopic liver resections were performed for metastatic tumors of colon cancer to the liver [27]. In our case the greater number of colon cancer metastases was due to the specific profile of our hospital department, which offers comprehensive treatment to patients with colorectal cancer. Metastases of malignant tumors from other organs can also be successfully treated using the laparoscopic technique according to the current indications.

Laparoscopic procedures for gallbladder cancer have been considered inappropriate for a long time. However, there is a growing body of evidence on the positive outcomes of laparoscopic procedures, especially in patients with a low stage of cancer. Outcomes are comparable to conventional surgeries performed to remove the gallbladder together with the adjacent hepatic parenchyma and combined with lymphadenectomy [10].

Most of our patients had anatomical resection of one or more segments of the liver. Despite many studies conducted to date, the advantages of anatomical or non-anatomical (wedge) resection have not been proven. A meta-analysis of 25 studies evaluating the efficacy of different types of liver resection due to HCC, comprising a population of 10,216 patients, showed the advantage of anatomical liver resection over wedge resections. The study also demonstrated a significant 5-year survival and Disease-Free Survival (DFS) advantage for patients undergoing anatomical resection compared to wedge resection. However, the study found no significant differences in mortality directly associated with the procedure between the two groups of patients [28]. Marubashi et al. [29] from Osaka Medical Centre conducted a study on 1,102 patients with HCC and showed no differences in the survival or incidence of postoperative complications, including mortality, between patients undergoing different types of resection. Undoubtedly, non-anatomical resections are parenchymal-sparing, which is especially important in patients with cirrhosis or other liver diseases. Reportedly, the key aspect when choosing the type of resection is to aim for the completeness of tumor resection, and the type of resection performed strongly depends on the tumor size and location.

Laparoscopic procedures were longer and associated with greater intraoperative blood loss compared to conventional open surgeries performed in our department. Currently, we observe a reduction in the duration of procedures and improvement in the results in terms of intraoperative blood loss. This is most likely due to the longer use of this technique and the surgical team gaining experience. A meta-analysis carried out by Tian et al. [30] based on 14 studies revealed no differences in operating time or mortality rate between patients undergoing laparoscopic and open liver resection for colorectal liver metastases. Nevertheless, the mean intraoperative blood loss was lower for laparoscopic resections. The largest systematic review of studies on the short-term benefits of laparoscopic liver resections in 9,527 patients, including 6,190 patients with malignant liver tumors, showed that laparoscopy was associated with fewer postoperative complications, shorter hospital stays and lower intraoperative blood

loss compared to open resections [6]. Researchers from John Hopkins University pointed out the lower incidence of postoperative wound infections, less need for blood transfusions, and lower risk of biliary leaks, pulmonary embolism and postoperative liver failure [31]. Reducing the risk of postoperative complications in elderly patients (especially those aged 75 years and older) by using the laparoscopic resection of liver tumors is of particular importance. These patients, due to their age and high incidence of comorbidities, are a special risk group for open surgeries [32].

Conclusion

Laparoscopic liver resections are becoming increasingly popular. These procedures reduce intraoperative trauma, minimize blood loss, and shorten hospitalization time and recovery. A particular advantage of laparoscopic surgery is observed in patients with cirrhosis, the elderly, and patients with coexisting internal diseases.

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