Laparoscopic liver resection for colorectal metastases – results of treatment

Arpad Ivanecz, Vid Pivec, Irena Plahuta, Bojan Krebs, Tomaž Jagrič, Stojan Potrč

Department of abdominal and general surgery, Division of surgery, University medical centre Maribor

Correspondence:
Arpad Ivanecz,
e: arpad.ivanecz@ukc-mb.si

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Abstract

Background: In many referral centres, laparoscopic liver resection (LLR) is a well-established method for the management of colorectal liver metastases (CLM). The aim of this study was to review a single institution experience.

Methods: Between April 2008 and September 2016, 58 patients underwent LLR for various benign and malignant liver tumours. The analysis included 12 patients operated for CLM. The primary outcomes of this prospective non-randomized study included operative procedure and operating time (minutes), estimated blood loss (mL), conversion rate, R0 resections, resection margins (mm), length of hospital stay (days), post-operative morbidity, and mortality. The secondary outcome of the study was survival analysis.

Results: Eight patients (67 %) underwent atypical LLR. The mean operating time was 130 minutes (range 60–210 minutes), and the mean estimated blood loss was 140 mL (range < 50–600 mL). In one patient LLR was converted to open procedure (conversion rate 8 %). Seven patients (58 %) had one liver metastasis. The mean size of metastases was 3.6 cm (range 1–9 cm). R0 resection was achieved in all cases. The mean resection margin was 6.8 mm (range 2–15 mm). The mean length of hospital stay was 6 days (range 3–12 days). Morbidity and mortality were 0 %. The median follow-up for surviving patients was 13 months. Nine patients are alive with no evidence of disease, two patients are alive with disease and one patient died of disease.

Conclusion: LLR is feasible and safe for the treatment of CLM, and there is no compromise of oncological surgical principles.

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Introduction

Liver resection is the only treatment possibility providing long-term survival in patients with colorectal liver metastases (CLM). The initiation of effective systemic therapy with chemotherapy and biological medicines improved the results of treatment. According to recently published literature, the overall 5-year survival rate of carefully selected patients could be up to 60 % (1). Advancements in surgical techniques and anaesthetic management have resulted in diminished post-operative mortality, which is less than 4 % in modern series. However, liver resection is still associated with rather high post-operative morbidity (up to 30 % of cases) such as wound complications, bleeding, cardio-

respiratory distress, bile leak, liver and kidney insufficiency (2).

Laparoscopic surgery is now established as the standard of care for a number of surgical procedures and its advantages are well-known. Theoretically, minimally invasive surgery is supposed to improve the results of treating CLM due to its potentially lower rate of postoperative morbidity and mortality. First laparoscopic liver resections (LLRs) were done in the early 1990s. Initially, this procedure was limited to the patients with symptomatic benign liver tumors. Soon the role of LLR was extended to malignant diseases. The LLR was acknowledged as a safe and feasible technique in 2008, after the conference in Louisville, USA (3). Since then, the number of LLRs has rapidly increased worldwide. The second consensus conference on LLR was held in Morioka, Japan, in 2014 after which the minimally invasive liver surgery was gradually recognized and was given an important place in modern surgical centres (4). Despite worldwide recognition of the benefits of LLR, there is still no prospective randomized trial to prove its advantages in the therapy of CLM. The latest meta-analysis published by Hallet et al in 2016 (5) summed up the results of eight different authors who compared LLR to open liver resection in retrospective series (6-13).

The experiences of Slovene authors were first presented at the 4th Congress of Endoscopic Surgery of Slovenia in 1997. Sever et al from University Medical Centre (UMC) Ljubljana reported laparoscopic pericystectomy of echinococcal cyst in 3rd liver segment (14). The pioneering work was continued, and Sojar et al reported an anatomical liver resection at the 6th Congress of Endoscopical Surgery of Slovenia in 2001; laparoscopic left lobectomy was performed on a young woman presented with symptomatic focal nodular hyperplasia (15). The same year, Sojar et al published the first Slovenian article on this topic in *Endoscopic Review*, meticulously describing 25 patients in whom LLR was performed for symptomatic benign liver tumours (16). At the time it was a large case series, while laparoscopic surgery was about to make its way toward recognition worldwide as well. In our institution, LLR was started in 2008; the first experiences in the treatment of malignant disease were published in 2011 (17). Experiences with LLR for different benign and malignant diseases were presented by the authors from UMC Ljubljana and UMC Maribor at the 13th Congress of Endoscopic Surgery of Slovenia in 2015 (18-19).

Until now, there has been no detailed analysis of LLR for CLM in Slovenia. The aim of this study was to present a single institution experience with LLR treatment of CLM, and to compare it to referral world centres.

Methods

LLR was started in the UMC Maribor in 2008. According to the recommendation guidelines of the Louisville Conference in 2008, small, mainly benign symptomatic tumors located in the accessible anterolateral segments of the liver were removed (3). With gradually increased skills, the indications spread to larger and even malignant tumours. More recently, technically demanding anatomical liver resection and simultaneous resection of the liver and colon or rectum have been performed. From the very beginning, LLRs were exclusively laparoscopic; they were not hand-assisted and the hybrid technique was not used.

Total LLR was performed on 58 patients in the period from April 2008 until September 2016, of which 12 patients

were operated for CLM, and were included in this prospective non-randomised study. The first LLR for CLM was done in May 2012.

Descriptive statistical methods were used. The primary aims of the study were to define the type and duration time of operation (minutes), estimated blood loss (mL), conversion rate, postoperative complications (90-day morbidity rate of grade ≥ 3 complications according to the Clavien-Dindo classification), Ro resection margins (mm), and length of hospital stay (days). "Morioka Classification" was used to assess the difficulty of LLR (20). It is a grading system evaluating LLR from 1 to 10 with three levels of difficulty. These are low (1-3), intermediate (4-6) and high (7-10). The secondary aims of the study were overall survival (OS) and disease-free survival (DFS).

Results

The characteristics of the 12 patients are presented in *Table 1*. The mean patient age was 61 years (range 49–81 years), seven of them were male (58 %). Seven patients (58 %) had one liver metastasis, five had two metastases (the mean number of metastases was 1.4). The mean diameter of the metastasis was 3.6 cm (range 1–9 cm). In most patients, metastases were located in the accessible anterolateral segments of the liver (segments 2, 3, 4b, 5, 6). In two patients (16 %), metastases were located in less favourable posterosuperior segments 4a and 8. Atypical liver resection was performed in eight patients (67 %) preserving as much healthy liver parenchyma as possible. Anatomical liver resection was performed in four patients (33 %): left

Table 1: Characteristics of patients who underwent LLR for CLM from the year 2012 until September 2016.

P	TUM number	Size (cm)	Segment	Type of resection	Difficulty of LLR "Morioka Score"	rr (mm)	CRC stage	HOSP (days)	Year	Vital status
1*	1	1	5	ATP	low (1)	5	T3N1M1	7	4	NED
2	1	1.2	2	ATP	low (1)	12	T3N1M0	3	3,5	AWD
3*	1	1.3	3	ATP	low (1)	5	T3N2bM1	42	1	DOD
4	2	1–2.5	2/3	2 x ATP	low (3)	15	T3N1aM0	3	3	AWD
5*	2	3–5	2/3	LLS	IM (4)	4	T3N1M1	7	2,5	NED
6	1	1	4b	ATP	low (1)	2 (CR)	T3N0M0	4	2	NED
7	1	2	6	SEGM	IM (4)	12	T3N0M0	5	1	NED
8*	1	1	2	LLS	IM (4)	10 (CR)	T2N0M1	9	1	NED
9	2	2–5	4b/8	2 x ATP	IM (5)	3	T3N0M0	7	< 1	NED
10	2	2–3	5/6	2 x ATP	IM (5)	2	T3N2bM0	5	< 1	NED
11*	2	3–2	4a/5	2 x ATP	IM (4)	6	T3N2bM1	12	< 1	NED
12	1	9	2/3	LLS	IM (6)	8	T3N0M0	5	< 1	NED

*Legend: P: patient; *: patients with simultaneous resection of primary CRC and liver metastases; TUM: tumour; rr: resection margin; CRC: colorectal cancer; LLR: laparoscopic liver resection; HOSP: length of hospital stay; ATP: atypical – non-anatomical; LLS: left lateral sectionectomy; SEGM: segmental liver resection; IM: intermediate; CR: Complete response; NED: No evidence of disease; AWD: Alive with disease; DOD: Dead of disease.*

lateral sectionectomy in three, and segmentectomy 6 in one patient.

In all cases, the metastases were removed along with the surrounding healthy tissue with a potentially curative Ro resection. When estimating the resection margin, the nearest resection margin was evaluated in the case of two metastases. Two patients had complete response to chemotherapy – the metastases seen on diagnostic imaging were not found on pathologic examination; there was fibrosis or complete necrosis at the site of previous metastases. In these cases, the resection margin was measured from these changes. The mean resection margin was 6.8 mm (range 2–15 mm). The mean duration of surgery was 130 min (range 60–210 min). The assessment of the difficulty of LLR according to the Morioka Score is given in *Table 1*. The mean estimated blood loss was 140 mL (range < 50–600 mL). Blood transfusion was required in two patients due to lower starting point of haemoglobin (89 and 95 g/L, respectively). The initial staging of the CRC before LLR is given in *Table 1*. In five patients (41 %) with synchronous liver metastases (patients 1, 3, 5, 8, 11) simultaneous operation of the primary CRC was performed (right hemicolectomy, resection of sigmoid colon, low anterior resection (two cases) and abdominoperineal resection)).

Table 2: Summary of liver resections performed in 8 centers worldwide.

Author, State	Period	Study design	Compared groups	N	Synchronous CLM (%)	Number of CLM average	Size of CLM (cm) average	Major resection (%)
Montalti et al (6), Belgium	2006–2012	MCS	LLR/OLR	57/57	54/49	NP	NP	23/23
Iwahashi et al (7), Japan	2007–2012	MCS	LLR/ OLR	21/21	57/57	1.8/2.1	2.4/2.6	14/9
Cheung et al (8), Hong Kong	2002–2011	MCS	LLR/ OLR	20/40	NP	1/1	1.5/2.2	5/5
Guerron et al (9), USA	2006–2012	MCS	LLR/ OLR	40/40	27/45	1.3/1.7	3.3/3.2	12/22
Cannon et al (10), USA	1995–2010	MCS	LLR/ OLR	35/140	9/9	1/1	4/5	54/51
Topal et al (11), Belgium	2001–2008	RCS	LLR/ OLR	81/193	10/29	2/2	4/3.2	22/42
Castaing et al (12), France	1997–2007	MCS	LLR/ OLR	60/60	12/12	2.2/2.2	3.3/4.4	43/41
This study, Slovenia	2012–2016	Case series	Not compared to OLR	12	42	1.4	3.6	0

Major resection: resection of ≥ 3 liver segments; LLR: laparoscopic liver resection; OLR: open liver resection; MCS: matched cohort study; RCS: retrospective cohort study; NP: not presented; CLM: colorectal liver metastases.

Conversion to open procedure was made in one patient (patient 9), with conversion rate of 8 %. In this case, the metastasis from the segment 4b was removed laparoscopically. After initial attempt to approach the technically challenging segment 8, conversion to open procedure was made. The reason for conversion was the concern about uncertain resection margin. LLR resulted in no post-operative complications. Abscess formation in the lesser pelvis (Clavien-Dindo grade IIIb complication) was a consequence of simultaneous laparoscopic colorectal surgery. Prolonged postoperative hospital stay was required only in this patient (42 days); for the remaining 11 patients the meanlength of hospital stay was 6 days (range 3–12 days). None of the patients died after surgery (post-operative mortality rate: 0 %). The median time of follow-up was 13 months (range 1–52 months). The vital status of our patients was evaluated in September 2016 and is shown in Table 1.

Discussion

In this study, the results of treating CLM by LLR in our department were analysed and compared to those of some well-known centres (*Table 2*). Our first LLR for this indication was made in 2012, whereas the selected referral centres worldwide performed such procedures for CLM at least ten years earlier (8,11-12). In our laparoscopic series twelve patients were treated for CLM, which is fewer than in other reported centres where the number of operated patients ranged from 20 to 80 (6-12). Otherwise in some of the leading centres the number of LLR for CLM surpasses the number of 500 (21).

Although potential advantages of LLR have been recognized by many surgeons, there still exist large centres which favour open surgery, for example Basingstoke in UK. In their study they concluded that patients, who would be appropriate for LLR were basically more suitable candidates for surgical procedure (13). Therefore, better results of LLR could be based on the selection of patients with more favourable prognostic factors (e.g. lower number and size of metastases). No doubt, this observation is also true for the patients presented in our study: most of them had only one metastasis (maximally two), metastases were quite small in diameter (all but one ≤ 5 cm) that were located in rather accessible anterolateral liver segments (segments 2, 3, 4b in 6). In the patient with metastasis in the posterosuperior part of the liver (segment 8) conversion was made. The difficulty of LLR is objectively measured by recently proposed scoring system, namely the "Morioka Score", where three categories are given: low, intermediate and high level of difficulty (20). According to this scoring, the procedures included in our study were assigned low-to-intermediate difficulty score.

The retrospective analyses of LLR compared to open surgery by methods of matched cohort study (6-10,12) or retrospective cohort study (11) were focused on two aims: short-term outcomes after surgery and oncological results. When considering short-term outcomes, LLR has some advantages over open surgery, which is objectively proven through reduced blood loss and lower rate of post-operative complications (5).

Along with improved surgical technique, the effect of pneumoperitoneum, which is absent in open surgery, contributes to reduced blood loss. The shorter length of hospitalisation was also found in some studies (11). These outcomes were confirmed in our study. Blood transfusion was given only to two patients (due to anaemia which was present already

before LLR) and there were no complications related to liver surgery. The length of hospitalisation was generally shorter, however, it should be noted that five patients with synchronous metastases underwent simultaneous procedures (primary CRC was removed concurrently) which prolonged hospitalisation. There was no difference in other parameters of short-term outcomes – duration of procedure compared to open surgery in all researches was the same (6-12). The mean duration of surgery of 130 minutes in our analysis was comparable to the usual duration of matching open liver resections. In several studies there was no difference in post-operative mortality rate, where 0 % was reported for both LLR and open procedures (10-12). In our series of LLRs post-operative mortality was 0 % as well.

In the analyzed reports there was no difference in oncological outcome of treatment, considering the following parameters: width of resection margins, rate of R0 resections(complete removal of the tumors with a clear microscopic margin and without residual tumors) (5-13). In our study, these results were confirmed: in all the patients R0 resection was made, the mean width of resection margin was 6.8 mm, and it was ≥ 2 mm in all patients. Experience with open procedures revealed that survival of patients with resection margin < 1 mm is comparable to survival of patients where this margin is ≥ 10 mm. In a large series in one of the world most experienced centres in the field of LLR in Oslo, Norway, this fact was recently confirmed for laparoscopy as well (22).

When compared to open procedures, no difference in 5-year OS and DFS were reported (5-13). Our survival analysis is momentarily incomplete, since we started in 2012 and most of the patients presented in this study were operated afterwards, thus the median follow-up period is too short (13 months). However, only one patient died of the disease.

The present study is subjected to several limitations. The first involves its small sample size, therefore it is only a case series. Secondly, the results were not compared to open procedures, thus the selection of patients with favourable prognostic factors for LLR might have influenced superior outcomes. Thirdly, the post-operative follow-up period has been too short to calculate long-term survival. Conclusions might be biased owing to these limitations.

It should be noted that in prestigious world journals the outcomes are presented by highly selected, topmost institutions which are leaders in this field. However, it is interesting to overview the results at the national level. What happens, when we look at all institutions which perform liver surgery in a region? In the national research study from France where laparoscopy is traditionally in favour it has been found that the LLR rate is surprisingly low – 25 % in some selected centres, but only 14 % when taking all centres into account (23).

Regardless of the indication the rate of LLR compared to all liver resections reaches 15 % in our institution. The option of a simultaneous operation of CRC has been considered our advantage. Some highly-specialised centres for liver surgery do not have this possibility, since colorectal surgeons are on separated and remote wards (personal communication with B. Edwin and M. Abu Hilal). It is one of the reasons that the number of these procedures is small in the literature. In a review article, Lupinacci et al describes 39 simultaneous laparoscopic procedures which have been published in 14 different articles (24). Therefore, our five simultaneous resections is not a small series at all.

Besides well-known advantages of laparoscopy its favourable impact on oncogenesis has been recently investigated. Presumably, it is consequence of less extensive stress response of organism (25). The results of the first prospective randomised controlled trial (The Oslo-CoMet Study) comparing LLRs vs. open procedures will be published soon (26). This well designed study will certainly have adequate statistical power, and hopefully the question of whether LLRs are better from open procedures will be finally answered.

Conclusion

In summary, LLR is a feasible, safe and effective treatment of CLM in well selected patients. This method offers several short-term advantages but exclusively in the hands of experienced surgeons. Very importantly, oncological results are not compromised since Ro resection with adequate width of resection margins are done in all patients. However, the outcomes of long-term survival are to be provided within the next few years.

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