

Colorectal cancer liver metastases: laparoscopic and open radiofrequency-assisted surgery

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Abstract

Introduction: The liver is the most common site of colorectal metastases (colorectal liver metastases – CLM). Surgical treatment in combination with oncological therapy is the only potentially curative method. Unfortunately, only 10–25% of patients are suitable for surgery. Traditionally, open liver resection (OLR) is usually performed. However, laparoscopic liver resection (LLR) has become popular worldwide in the last two decades.

Aim: To evaluate the effectiveness and benefits of radiofrequency minor LLR of CLM in comparison with OLR.

Material and methods: The indication for surgery was CLM and the possibility to perform minor laparoscopic or OLR not exceeding two hepatic segments according to Couinaud's classification.

Results: Sixty-six minor liver resections for CLM were performed. Twenty-five (37.9%) patients underwent a laparoscopic approach and 41 (62.1%) patients underwent OLR. The mean operative time was 166.4 min for LLR and 166.8 min for OLR. Average blood loss was 132.3 ± 218.0 ml during LLR and 149.5 ± 277.5 ml during OLR. Length of hospital stay was 8.4 ± 2.0 days for LLR and 10.5 ± 5.8 days for OLR. All resections were R0. There was no case of mortality. Postoperative complications were recognized in 9 (13.6%) patients: 8 in the group of OLR patients and 1 in the LLR group. The median survival time for LLR was 70.5 months and for OLR 61.9 months. The 5-year overall survival rate was higher for LLR vs. OLR – 82.1% vs. 69.8%. The average length of disease-free interval after LLR was greater (52.2 months) in comparison with OLR (49.4%). The 5-year disease-free interval was 63.2% for LLR and 58% for OLR.

Conclusions: Outcomes and oncological radicality of minor laparoscopic liver resections of CLM are comparable to outcomes of OLR.

Key words: colorectal cancer, liver metastases, laparoscopic liver resection, radiofrequency.

Introduction

The liver is the most common site of colorectal cancer metastases. Approximately 20% of patients suffering from colorectal cancer have liver metastases at the time of diagnosis; the other 30–40% of

patients will develop them in the following postoperative period [1]. The median survival in patients with untreated colorectal cancer is in the range of 6–9 months, and 5-year survival is rather rare, ranging from 0 to 3% [2–4]. It is still true that surgical treatment in combination with oncological therapy

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is the only potentially curative treatment modality. The result is 5-year survival of 16–74% and 10-year survival of 9–69% in patients after R0 resection [5]. Unfortunately, only 10–25% of patients meet the criteria for implementation of R0 surgical resection at the time of diagnosis [6].

Aim

The aim of this prospective study was to evaluate the effectiveness and benefits of radiofrequency minor laparoscopic liver resection (LLR) in the treatment of colorectal liver metastases (CLM). Minor laparoscopic resection was determined as a resection not exceeding more than 2 segments according to Couinaud's classification. The hypothesis of the study was that LLR can be compared with open liver resection (OLR) and statistically does not differ in the following monitored parameters: operating time, intraoperative blood loss, postoperative days spent in the intensive care unit (ICU) and hospital stay, amount of drainage in the first 2 days, duration to abdominal drain removal, postoperative complications, overall survival and disease-free interval.

Material and methods

Sixty-six patients with CLM not exceeding two hepatic segments were included in the study. Inclusion criteria were as follows: age over 18 years and the possibility to perform laparoscopic or open liver resection not exceeding two hepatic segments.

Exclusion criteria were as follows: technically unresectable hepatic lesions, hepatic lesions exceeding more than 2 segments, extrahepatic dissemination, metastasis of non-colorectal origin and patient unfit for surgery (ASA IV or more).

All eligible patients underwent a preoperative interview with the operating surgeon, physical examination, basic laboratory tests, carcinoembryonic antigen (CEA) determination, spiral computed tomography (CT) or magnetic resonance imaging (MRI) of the abdomen to assess the metastatic process accurately, chest X-ray, and anaesthetic preoperative examination. The minor laparoscopic procedures ranged from a simple local metastasectomy (wedge resection) through segmentectomy to bisegmentectomy. Postoperatively, patients were followed at the outpatient department.

Data were analysed using the MySQL database version 5 January 32 (Oracle, Redwood Shore, CA,

USA), SPSS statistical software version 18 (IBM, Rochester, MN, USA) and Statgraphics Centurion XV. Then Microsoft Excel 2007 (Microsoft, Redmond, WA, USA) and computer applet IO_binom.xlsx were used.

Statistical analysis

Descriptive statistics were used to determine the basic characteristics of the sample. The chi-square test (χ^2) was used to determine whether the data were distributed normally. The Mann-Whitney test was used to test differences between single groups (normal distribution was not observed). Kaplan-Meier curves (log rank, Breslow and Tarone-Ware tests) were used to determine differences in overall survival and identification of disease-free interval. The level of significance of 0.05 was set for all tests [7].

Results

A laparoscopic operation was performed in 25 (37.9%) patients, and 41 (62.1%) patients underwent conventional open surgery. Mean operative time was 166.4 min (50–370 min) for LLR and 166.8 min (80–335 min) for OLR. Blood loss during surgery was 132.3 ± 218 ml after LLR and 149.5 ± 277.5 ml after OLR. Number of days of hospitalization in the ICU was 3.0 ± 1.9 days (0–7 days) for LLR and 3.4 ± 1.8 days (0–7) for OLR. Length of hospital stay was 8.4 ± 2 days for LLR and 10.5 ± 5.8 days for OLR. Secretion from the abdominal drain on the first postoperative day was 82.5 ± 116.2 ml after LLR and 47.2 ± 63.3 ml after OLR. The abdominal drain was removed 4.7 ± 1.9 days after LLR and 6.2 ± 6.1 days after OLR.

Statistical evaluation has shown that there was not a statistically significant difference between LLR and OLR in terms of the operation time, perioperative blood loss, number of days in the postoperative ICU, length of stay in hospital (Table I), the amount of secretion from the abdominal drain or the average number of days to abdominal drain removal.

Postoperative complications occurred in 9 (13.6%) patients. There were 8 (19.5%) complications (pneumonia, wound infection, respiratory failure, bile leak [2x], hematoma, liver abscess, urinary infection) in the group of patients undergoing OLR and only 1 (4%) (wound infection) in the group of patients undergoing LLR. This difference in postoperative complications was statistically significant ($p = 0.038$).

The average survival time for LLR was 70.5 months and for OLR was 61.9 months. The 5-year

Table I. Comparison of the monitored parameters in LLR and OLR groups of patients

Parameter	Age [years]		Operative time [min]		Blood loss [ml]		Length of stay in intensive care unit [days]		Length of stay in hospital [days]	
	Type of operative approach									
	LLR	OLR	LLR	OLR	LLR	OLR	LLR	OLR	LLR	OLR
Mean	62.1	61.3	166.4	166.8	132.3	149.5	3	3.4	8.4	10.5
Median	63	64	171	160	50	57.5	2	4	8	8
Standard deviation	10.3	9.7	81.5	59	218	277.5	1.9	1.8	2	5.8
Sig.	NS, $p = 0.381$		NS, $p = 0.492$		NS, $p = 0.422$		NS, $p = 0.136$		NS, $p = 0.291$	

Table II. Summary for survival time based on the type of surgery. Values of p for the individual tests in the assessment of the statistical difference in survival

Operative approach	Mean survival time [months]	5-year survival (%)	Test p -value		
			Log rank	Breslow	Tarone-Ware
Laparoscopic	70.5	82.1	0.398	0.413	0.402
Open	61.9	69.8			

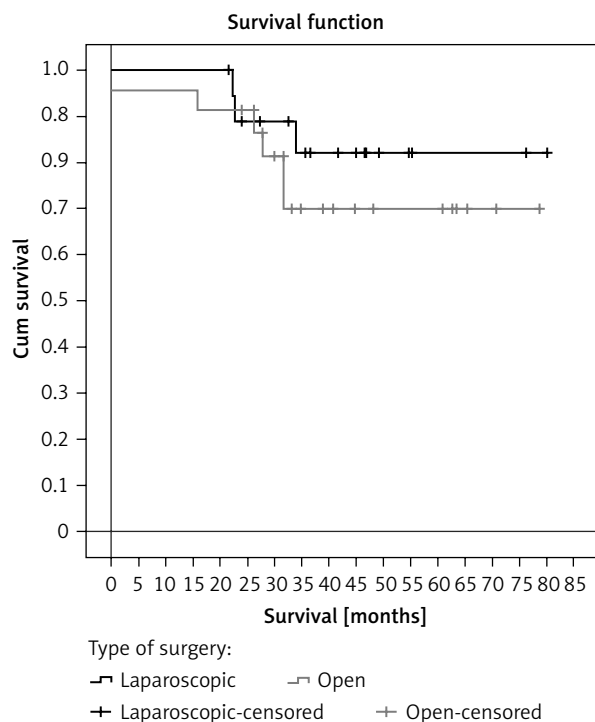
overall survival rate was higher for LLR versus OLR – 82.1% vs. 69.8% (Table II, Figure 1). Based on log rank, Breslow and Tarone-Ware tests, no statistically significant difference was found. According to the tests, there was no difference in the overall survival of patients with CLM depending on the type of surgery – LLR or OLR.

The average length of disease-free interval for LLR was greater (52.2 months) in comparison with OLR (49.4 months). The 5-year disease-free interval was for LLR 63.2% and for OLR 58.0% (Table III, Figure 2). Statistical evaluation revealed no difference in disease-free interval in patients with CLM depending on the operative approach – laparoscopic or open.

Discussion

In 1993, Gagner *et al.* [8] performed the first laparoscopic liver resection. The following two decades meant rapid development of laparoscopy [9]. Nowadays, the number and rate of laparoscopic liver procedures are still increasing. Generally, the proportion of laparoscopic procedures in liver surgery is reported between 5% and 30% [10–13]. In several major world centres the proportion of laparoscopic procedures is higher – around 50–80% [14–17].

In 2011, Nguen *et al.* [18] reported his experience with a total of 1294 patients. Three hundred and fourteen (24.3%) of them were operated on laparo-

**Figure 1.** Kaplan-Meier survival curves for patients with CLM and R0 resections according to operative approach

scopically. Han *et al.* [19] reported 386 liver resections in their statistical evaluation within 5 years; 170 (44%) were performed laparoscopically. In this

Table III. Summary for disease-free interval based on type of surgery. Values of *p* for the individual tests in the assessment of the statistical difference in survival

Operative approach	Mean disease-free interval [months]	5-year disease-free interval (%)	Test <i>p</i> -value		
			Log rank	Breslow	Tarone-Ware
Laparoscopic	52.2	63.2	0.674	0.570	0.624
Open	49.4	58.0			

study conducted at the University Hospital Ostrava, the proportion of LLR was 35.9%. This is a fairly significant proportion, which is determined by the historical focus on minimally invasive procedures and the possibility of using advanced laparoscopic techniques [20, 21].

Indication criteria for the application of LLR are not clearly established. It depends particularly on the size and location of metastases. It is also necessary to take into account previous surgery, patient's condition and comorbidities, surgeon's experience and workplace customs. Generally, smaller metastases located in the anterolateral segments S2-6 are considered optimal for the laparoscopic approach. Conversely, metastases bigger than 6 cm, their penetration into surrounding structures or location near

the hepatic hilum, vena cava or in postero-superior segments S1, S4a, S7 and S8 are considered inappropriate for laparoscopy [22, 23]. However, Cho *et al.* reported a series of 36 patients with lesions in the postero-superior segment (S7, 8, 4a and 1) treated only with the laparoscopic approach [17, 24]. The role of laparoscopy for tumours requiring resection of postero-superior segments should be sufficiently specified in the future.

The number of patients in published studies varies widely. There are studies with a small number of patients [25–28]. On the other hand, there are studies with a much larger group of patients – Nguyen *et al.* evaluated 314 patients [18], Koffron *et al.* 300 patients [16]. In 2007 Simillis *et al.* [29] published the results of a meta-analysis comparing LLR with OLR. In the group of patients studied at the University Hospital Ostrava, there were 66 patients with CLM, and 25 patients were operated on laparoscopically. The number of patients is comparable with the middle of the spectrum in individual studies in the world literature.

Length of hospital stay in our study was 8.4 ± 2 days after LLR and 10.5 ± 5.8 days after OLR. In comparison of laparoscopic and open liver resection, there was no significant difference in favour of laparoscopic surgery. Our length of hospital stay is the average length of hospital stay after laparoscopic resections reported in studies from Europe, which ranges between 3.5 and 10 days [27, 30–42]. The average length of hospital stay differed greatly among individual studies. As regards the duration of hospital stay after liver resection, there is a very interesting comparison of local customs and traditions. Studies published in the USA [14, 16, 43, 44] indicate an average length of hospital stay of 1.9–4 days after LLR, while above-mentioned European studies report 3.5–10 days. Studies published in Asia indicate the length of hospital stay much longer, between 4 and 20 days [45–52]. However, the trend was consistent regardless of continents and pointed to a shorter length of hospital stay in the group of LLR compared to OLR. It

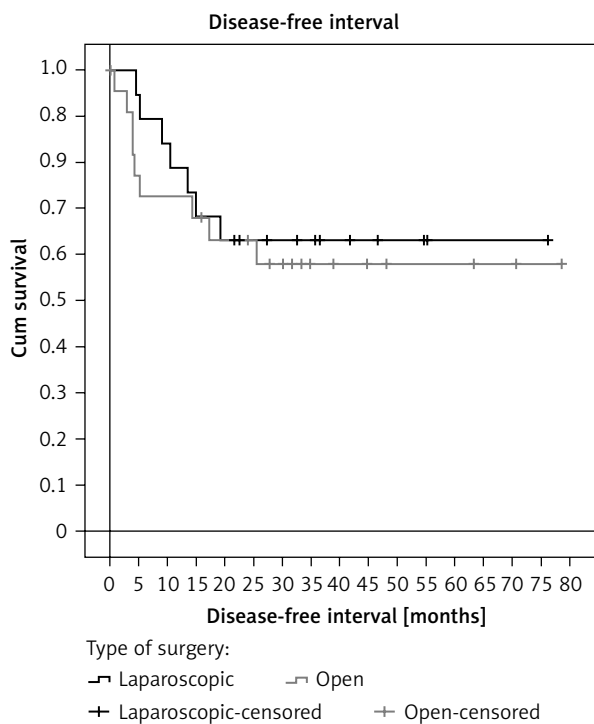


Figure 2. Kaplan-Meier disease-free curves for patients with CLM and R0 resections according to operative approach

should be noted that although the length of hospital stay was in our study shorter after laparoscopic operations, the results in favour of laparoscopy were not statistically significant.

The average number of days of hospitalization in the ICU in our study was 3.0 days for LLR and 3.4 days for OLR. Statistical evaluation found no difference. Abu Hilal *et al.* compared the results of right-sided hemihepatectomy performed laparoscopically (36 patients) and openly (34 patients). He compared the duration of hospitalization in an ICU, where the median was 2 days vs. 4 days ($p < 0.0001$) and the total hospitalization period (5 days vs. 9 days, $p < 0.0001$) was significantly shorter in the group of patients treated laparoscopically [53].

At the beginning of laparoscopic resection, significantly longer operating time was stated as one of the main disadvantages in comparison with open resection [39, 42, 43]. The development of laparoscopy and surgical techniques compensated this difference gradually. In our study, similarly to many other studies [15, 27, 30, 35], a significant difference in operating time was not found. On the other hand, there are studies proving shorter operating time of the laparoscopic approach [14, 16, 32]. These differences may be caused by the method of liver transection, with authors using the harmonic scalpel reporting a longer operating time, while authors using endostaplers reported a shorter operating time.

Laparoscopy is considered to be a miniinvasive and gentle method. Most studies show significantly lower intraoperative blood loss compared to the open approach [11, 14, 30, 43, 48, 54]. In our study significant differences between blood loss during laparoscopic surgery compared to losses in open procedures ($p = 0.422$) were not found. Generally, it is considered that blood loss should be smaller in the laparoscopic approach because of better visualization of the operative field, careful dissection by laparoscopic instruments, established pneumoperitoneum and reduced blood loss through laparoscopic wounds [55].

Monitoring of postoperative morbidity and mortality is one of the main indicators of the effect of laparoscopic treatment. While many studies have shown a comparable amount of postoperative complications between LLR and OLR, there are also studies [11, 27, 32, 34, 35, 44, 54] showing a significantly lower incidence of complications after laparoscopic operations (6–13.8%) compared to the number of complications after open procedures (28.9% to

47.8%). There were no differences in perioperative mortality between the two groups of patients in these trials. Our study belongs to the category of studies with lower postoperative morbidity (4.0%) during laparoscopic operations (compared to patients operated openly 19.5%). The relatively favourable outcome of complications after laparoscopic resection is fully consistent with the results of other authors in the world literature in recent years [56]. Lee *et al.* reported a 4% complication rate in laparoscopic resection [48], Shimada *et al.* [49] 5.9%, Rowe *et al.* [54] and Rau *et al.* [40] 6%, Topal *et al.* 8% [11]. These results demonstrate significant progress in the development of technology and operational skills of surgeons. Mizuguchi *et al.* [57] found postoperative morbidity to be significantly lower in patients operated on laparoscopically, ranging from 5.9% (47) to 34.2% [42], while in OLR it ranged from 6.7% [33] to 47.8% [34].

The key question is oncological radicality after laparoscopic surgery. Careful intraoperative manipulation, no-touch technique, the use of plastic bags to remove material from the abdominal cavity and others lead to prevention of port-site metastases [55]. Comparison of overall survival curves and disease-free interval is crucial. Many studies have found no significant difference in 3- and 5-year survival interval depending on the chosen approach (Table IV) [18]. Cai *et al.* reported survival of patients with HCC after laparoscopic resection as 95.4%, 67.5% and 56.2% after 1, 3 and 5 years, while survival was 100%, 73.8% and 53.8% after open resection [45]. Ito *et al.* found no significant difference in 3-year survival in patients with CLM operated on by an open or laparoscopic approach [43].

Five-year survival interval in our study was statistically evaluated using Kaplan-Meier curves. The 5-year survival rate for minor R0 resection for CLM was 82.1% for operations performed laparoscopically and 69.8% for operations performed openly. A statistical evaluation showed that there was no difference in survival interval depending on the selected operation – open or laparoscopic. Oncological radicality of laparoscopic surgery for CLM in our group of patients was comparable with the radicality of operations performed conventionally openly.

Conclusions

Our study showed that minor LLR of CLM was comparable with outcomes of procedures performed

Table IV. Overall survival after LLR vs. OLR for cancer in comparative studies

Source, year	Country	Tumour	Overall survival [%]		Follow-up [years]	Value of <i>p</i>
			LLR	OLR		
Kaneko <i>et al.</i> , 2005 [28]	Japan	HCC	61	62	5	NS
Cai <i>et al.</i> , 2008 [45]	China	Mix	50	51	5	NS
Belli <i>et al.</i> , 2009 [32]	Italy	HCC	67	61	3	NS
Ito <i>et al.</i> , 2009 [43]	US	CLM	72	56	3	NS
Lai <i>et al.</i> , 2009 [47]	Hong Kong	HCC	60	60	3	NS
Castaing <i>et al.</i> , 2009 [31]	France	CLM	64	56	5	NS
Endo <i>et al.</i> , 2009 [50]	Japan	HCC	57	48	5	NS
Sarpel <i>et al.</i> , 2009 [58]	US	HCC	95	75	5	NS
Tranchart <i>et al.</i> , 2010 [30]	France	HCC	46	37	5	NS
Vavra <i>et al.</i> , 2014	Czech	CLM	82	70	5	NS

openly. The oncological radicality of the laparoscopic approach for CLM not exceeding two hepatic segments was comparable with the conventional open surgery.

The indication for LLR does not differ from the indication for OLR. Patients with lesions in antero-lateral segments are suitable candidates for laparoscopy. Although many types of liver resection are nowadays feasible laparoscopically, major resection and resection of postero-superior segments should be reserved for experienced surgeons with experience in laparoscopic liver resections.

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Conflict of interest

The authors declare no conflict of interest.

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