



Research Article

Simultaneous Laparoscopic Resection of Primary Colorectal Cancer and Associated Liver Metastases: A Systematic Review

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Abstract

Purpose: To investigate the safety, feasibility and perioperative outcome of laparoscopic simultaneous resection of primary colorectal cancer with synchronous liver metastases.

Methods: We conducted a systematic search of all articles published on PubMed until August 2020. Search terms included: hepatectomy, liver resection, laparoscopy, hand-assisted laparoscopy, minimally invasive, colectomy, colorectal neoplasms, colorectal resections, combined resection and simultaneous resection. No randomized trials are available, all the data have been reported as case reports, case series or case-control studies.

Results: Six hundred and sixty-one laparoscopic simultaneous resections were identified in 22 reviewed articles. There were 93 (15 %) major hepatic resections. The most performed liver resections were parenchymal sparing non-anatomical resections. Colorectal resections included right colectomy, left colectomy, anterior resection and low anterior resection; majority of colorectal surgeries were rectal resections. According to the proposed reviewed data, the laparoscopic simultaneous resections appeared to be feasible and safe, even with major hepatectomies. Good experience of the surgeon and proper patient selection are the keys to successful results. Minor liver resections associated with colorectal resection can be routinely considered.

Keywords: Colorectal cancer; laparoscopic surgery and simultaneous resection; liver metastases

Introduction

Colorectal Cancer (CRC) is the third most deadly and fourth most commonly diagnosed cancer in the world [1]. Several decades ago, colorectal cancer was infrequently diagnosed. Nowadays, more than 900 000 deaths annually due to CRC [2]. Besides an ageing population and dietary habits of high-income countries, unfavorable risk factors such as obesity, lack of physical exercise, and smoking increase the risk of colorectal cancer [2]. The liver is the most common site of CRC metastasis. Synchronous Liver Metastases (SLMs) are found in up to 25% of CRC patients at time of diagnosis and up to 50% will develop metachronous metastases. Whereas, in third of metastatic CRC patients the disease is confined to the liver only and synchronicity had been correlated with poor prognosis [3-5]. Recent advances in chemotherapeutic

and biological agents and local therapies for liver-limited metastatic CRC have evolved in the treatment paradigm but the surgical resection remains the treatment of choice and had the only chance for long-term survival. The goal of surgery should be to resect all metastases with negative histological margins while preserving sufficient functional hepatic parenchyma [6]. Different open surgical strategies have been proposed to treat CRC with synchronous liver metastases. Among these, the simultaneous primary colon and liver resection has been showed to be safe and effective even when major hepatectomies are required [7].

Laparoscopic liver resection had started at the beginning of the 1990s, with the initial reports being published in 1991 and 1992. These were followed by reports of left lateral sectionectomy in 1996. In the years following, the procedures of LLR were expanded to hemi-hepatectomy, sectionectomy, segmentectomy and partial resection of posterosuperior segments, as well as the parenchymal preserving limited anatomical resection and modified anatomical

(extended and/or combining limited) resection procedures [8]. The potential benefits of a combined laparoscopic approach for primary CRC and liver metastasis include the possibility to perform a radical operation with small incisions, shorter hospital stay, earlier recovery and earlier adjuvant treatment [8]. The role of laparoscopy in the management of simultaneous colonic and liver resection for synchronous colorectal cancer was discussed in the Maiorka and Southampton consensus meeting. The experts agreed that there is insufficient comparative data for combined liver and colorectal resection, they agreed also that combined laparoscopic major liver resection and colonic resection are complex and lengthy procedures with the potential for increased operative risks [8,9].

Recently, many studies have been showed that the laparoscopic combined resection of colorectal cancer and is safe and effective as the open treatment for simultaneous resection of CRC with SLMs, and can be used for both minor and major liver resection with good post-operative outcomes and faster return to daily life [10-12]. To date, no randomized controlled trials have compared peri-operative and oncological outcome of laparoscopic and open simultaneous colonic and liver resection. To address this issue, we conducted a comprehensive systemic review of the studies that was published until August 2020.

Materials and Methods

Criteria for inclusion studies in this review

All the studies that described the clinical course of patients who underwent combined laparoscopic CRC and SLM resections (pure laparoscopy or hand assisted) and contained the measurements of post-operative outcome were included in the study. A synchronous metastasis was defined as a metastasis present at the time of the original colorectal resection. Liver resection was considered as any liver tissue resection, either major or minor resection. Colorectal surgery was considered if the primary tumor was completely resected.

Criteria for exclusion studies from this review

All the case reports were excluded from the study, in addition to the studies that investigated the non-simultaneous resections or any other pathologies rather than metastatic CRC to the liver.

Search strategy

A systematic search was conducted for laparoscopic simultaneous resection of primary CRC and liver metastasis. We searched Medline (through PubMed) for related literature until August 2020. Advanced searches were conducted for keywords

and text (title or abstract). Search terms included: hepatectomy, liver resection, laparoscopy, hand-assisted laparoscopy, surgical procedures, colectomy, colorectal neoplasms, and colorectal resections. A cross-reference search of review articles in leading journal was performed also.

Methods of review

Abstracts were reviewed by three different authors to assess whether the studies met the eligibility criteria. All studies considered to fit the study criteria were then analyzed by the authors (Figure 1).

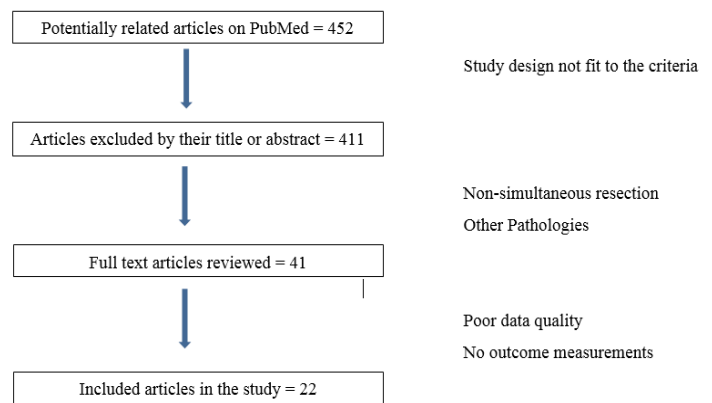


Figure 1: Literature Search.

Results

From 2005 to 2020, there were a total of 452 studies and abstracts that met the initial screening criteria of patients undergoing simultaneous resection of colorectal cancer and liver metastases. Among the studies that were screened, 22 studies met the inclusion criteria and were included in the analysis and no randomized trials were identified in the literature (Figure 1). All 22 studies had a retrospective study design with a total of 661 patients who underwent simultaneous resection of colorectal cancer and liver metastases were identified and included in the analytic study cohort. The individual cohort size for any given study varied from 4 to 142 patients. There were 350 (57%) males and 266 (43%) females, the age of patients going colorectal and hepatic resection was similar across the studies examined with a median age in the 60's (Table 1). Most of the studies (14, 64%) reported the patients BMI with a median of 23.7. In 497 patients ASA classification was reported, but there is no doubt that there was a bias in patients' selection because most of the patients (78%) were ASA I or II and only 22% were classified as ASA III or IV.

Authors	Year of Publication	# Patients	Type of Study	Age	BMI	Neoadjuvant Chemotherapy	ASA I / II	ASA III / IV
Shin et al. ¹¹	2019	126	CM	59±11	23±2.8	28 (22%)	120	6
Bizzoca et al. ¹²	2019	17	CS	56±12	24.6±5.1	NA	12	5
Chen et al. ¹³	2019	16	CM	NA	NA	NA	NA	NA
Ivanec et al. ¹⁹	2018	10	CS	62.2±7.9	26.9±.34	7 (70%)	6	4
Van der Poel et al. ²⁰	2018	61	CM	64±11.6	25.8±2.4	12 (20%)	48	13
Shim et al. ²¹	2018	22	CM	65.5±8.9	23.7±3.1	1 (5%)	22	0
Xu et al. ²²	2018	20	CM	58±2	NA	6 (30%)	20	0
Gorgun et al. ²³	2017	14	CM	56.3±3.3	25.1±.8	6 (43%)	0	14
Ratti et al. ²⁴	2016	25	CM	60±20	NA	20 (80%)	20	5
Ferretti et al. ¹⁵	2015	142	CM	66±19	24.3±6	NA	94	48
Berti et al. ²⁵	2015	35	CS	71±11	<30	NA	29	6
Inoue et al. ²⁶	2014	10	CS	60	22.4±1.9	1 (10%)	NA	NA
Ida et al. ²⁷	2014	10	CS	63.5	NA	2 (20%)	NA	NA
Jung et al. ²⁸	2014	24	CM	60	23.7	NA	11	3
Shampinato et al. ²⁹	2013	4	CS	61.5±7	25.1	1 (25%)	4	0
Hoekstra et al. ³⁰	2012	5	CS	68.8	NA	NA	NA	NA
Hu et al. ³¹	2012	13	CS	54±10	21.5±7.8	NA	NA	NA
Hayashi et al. ³²	2011	7	CS	58.6	NA	NA	NA	NA
Lee et al. ¹⁰	2010	10	CS	63.7±9.4	23.5±2.1	NA	NA	NA
Patriti et al. ³³	2009	7	CS	73	NA	4 (57%)	1	6
Polignano et al. ³⁴	2009	28	CS	68	NA	NA	NA	NA
Kim et al. ³⁵	2008	10	CS	59.5	22.5	NA	NA	NA
Total		661		61	23.7	88/309 (28%)	387 (78%)	110 (22%)

CM - Case matched study, CS- Case series study, BMI – body mass index, ASA - American society of anesthesiology

Table 1: Characteristics of the included studies.

Neoadjuvant chemotherapy treatment was reported in 11 (50%) studies that include 309 patients, of those surprisingly only 88 (28%) patients had received chemotherapy before the surgery. For example, Shin, et al. [11] reported only 28 (22%) from 126 patients received neoadjuvant chemotherapy. Most of the CRC were located in the rectum (44%) and the Low anterior resection was the most performed procedure, while the majority of hepatic resections (85%) were parenchymal sparing resections (Table 2). The exact surgical procedure was prescribed in about two third of the studies and most of them used to do liver resection first. About 94% of surgeries were done by pure laparoscopic technique and the rest of surgeries by hand assisted laparoscopic technique, the conversion rate was 2.7% due to the difficulty to complete the procedure or due to uncontrollable bleeding. Regarding the operation time, was ranged between 165 to 530 minutes, but it is difficult to explain this variation from the studies. The estimated blood loss also varied between the different publications with median of 250 m³l, but there is no date about blood transfusion.

Authors	# Pt	Colorectal Surgery			Liver Surgery		Pure lap	HALS*	Conv*	OR TIME (min)	EBL* (m ³ l)
		Right	Left	Rectal	Major	Minor					
Shin, et al.[11]	126	22	51	53	33	93	126	0	4	330	135
Bizzoca, et al.[12]	17	2	6	9	2	15	17	0	0	165	158
Chen, et al.[13]	16	4	0	12	0	16	16	0	1	320	369
Ivanecs, et al.[14]	10	3	3	4	0	10	10	0	0	261	105
Van der Poel, et al.[15]	61	18	31	12	0	61	55	6	3	206	200
Shim, et al.[16]	22	3	1	18	2	20	22	0	0	135	100
Xu, et al.[17]	20	8	7	5	4	16	20	0	0	175	246
Gorgun, et al.[18]	14	3	3	8	2	12	14	0	NA	321	347
Ratti, et al.[19]	25	5	8	12	6	19	25	0	0	420	350
Ferretti, et al.[20]	142	38	46	58	17	125	127	15	7	360	200
Berti, et al.[21]	35	10	9	16	0	35	350	0	NA	240	200
Inoue, et al.[22]	10	3	3	4	0	10	8	2	0	425	245
Ida, et al.[23]	10	2	3	5	0	10	10	0	0	550	400
Jung, et al.[24]	24	2	1	21	6	18	24	0	0	290	325
Shampinato et al.[25]	4	0	3	1	4	0	4	0	0	495	475
Hoekstra, et al.[26]	5	1	1	3	0	5	2	3	0	250	700
Hu, et al.[27]	13	3	4	6	4	9	13	0	0	313	259
Hayashi, et al.[28]	7	1	1	5	0	7	2	5	0	407	207
Lee, et al.[10]	10	4	0	6	1	9	10	0	1	401	500
Patriiti, et al.[29]	7	1	5	1	1	6	7	0	0	240	720
Polgnano, et al.[31]	28	12	7	9	5	23	28	0	NA	530	175
Kim, et al.[32]	10	2	3	5	6	4	0	10	0	439	350
Total	661	147 (24%)	196 (32%)	273 (44%)	93 (15%)	523 (85%)	581 (94%)	35 (6%)	16/584 (2.7%)	320	250

P: Patient; Pure lap: Pure Laparoscopy; HALS: Hand Assisted Laparoscopic Surgery; OR: Operative; EBL: Estimated Blood Loss

Table 2: Operative data.

Table 3 summarize the surgical pathology outcome, 72% of patients have lymph node metastases, but the studies lack the report of number of lymph nodes that was harvested. The majority of studies also included a large subset of patients (62%) with only a solitary (24%) metastasis and 17% of patients had three or more liver metastases. The median largest liver metastasis was 54 m³m with a range from 31 mm to 110 mm [18,19]. In addition to metastases number and size, location of the metastases may impact the type of liver resection but this wasn't reported in the studies. The free margins distance of the liver resection metastases wasn't reported. Post-operative complications and mortality were in acceptable ranges as described in Table 4. The bile leak rate was 2.8%, the colonic anastomosis leak was 4.3% and the 30 days mortality rate did not exceed 1%.

Authors	# Pt	LN Status			No Liver metastases			Size largest (m ³ m)
		N0	N1	N2	single	<3 mets	≥ 3 mets	
Shin et al. ¹¹	126	25	58	43	52	90	36	45
Bizzoca et al. ¹²	17	4	12	0	10	NA	NA	69
Chen et al. ¹⁹	61	NA	NA	NA	NA	NA	NA	NA
Ivanecy et al. ¹³	10	0	2	8	NA	10	0	32
Van der Poel et al. ²⁰	61	13	24	24	44	54	7	NA
Shim et al. ²¹	22	5	8	9	20	22	0	101
Xu et al. ²²	20	8	9	3	NA	14	6	45
Gorgun et al. ²³	14	4	7	3	12	14	0	31
Ratti et al. ²⁴	25	12	10	3	3	NA	NA	110
Ferretti et al. ¹⁴	142	54	44	44	107	120	22	100
Berti et al. ²⁵	35	14	10	11	17	27	8	Na
Inoue et al. ²⁶	10	NA	NA	NA	4	9	1	95
Ida et al. ²⁷	10	1	4	5	8	10	0	NA
Jung. et al. ²⁸	24	4	12	8	15	23	1	70
Shampinato et al. ²⁹	4	0	2	2	0	0	4	50
Hoekstra et al. ³⁰	5	3	1	1	3	4	1	70
Hu et al. ³¹	13	NA	NA	NA	NA	NA	NA	42
Hayashi et al. ³²	7	NA	NA	NA	7	7	0	35
Lee et al. ¹⁰	10	1	2	7	6	7	3	59
Patriti et al. ³³	7	NA	NA	NA	5	6	2	NA
Polignano et al. ³⁴	28	NA	NA	NA	20	25	3	NA
Kim et al. ³⁵	10	0	2	8	5	9	1	40
Total	661	148 (28%)	208 (39%)	179 (33%)	338 (62%)	451 (83%)	95 (17%)	54

LN: lymph node

Table 3: Pathology characteristics.

Discussion

Complete radical resection of the primary colorectal cancer and the metastatic liver lesions is the only potential curative treatment. The resection strategy for CRC and liver metastases include simultaneous resection and staged resection including colon resection first or liver resection first and between chemotherapy treatment. The one-stage approach for simultaneous colectomy and hepatectomy give the advantages to avoid two surgical procedures thus reducing the risk for patients while keeping acceptable morbidity and good oncological results. With the improvement in surgical technique and the surgical instruments, the minimal invasive surgery showed a great advantage in liver resection [8,9]. Reports regarding the safety and efficacy of combined resection of colon cancer and liver metastases have been increased but most of these publications were case series or limited by a small sample size [25,26,28,29]. The Southampton consensus meeting that took place in 2017, one of the topics that came up for discussion was simultaneous resection of colon and liver but due to insufficient comparative data for combined colon and liver resection there was no unequivocal recommendation due to the fear of an increase in the morbidity and mortality rate [9]. Since the consensus conference, a number of studies has been published with a reasonable number of patients [11-18].

In the present study perioperative outcomes of 661 patients, affected by stage IV CRC treated with simultaneous laparoscopic colon and liver resection up to August 2020, were retrospectively analyzed. The median age of the cohort study was 60 but in part of the studies even younger [12,17,18,27]. Obesity is one of the significant causes of fatty liver or steatosis that is a risk factor for morbidity after liver resection, in the present study the range of body mass index was 21 to 27 with median of 23. Surprisingly 78% of the patients in the present study were classified as ASA I or II. There is no doubt that there is a selection bias of patients for simultaneous colon and liver resection as this is reflected in the age, BMI and ASA classifications of the patients. In this review, many different aspects of combined laparoscopic colorectal and liver resections have been evaluated, such as its feasibility, safety, efficacy and short-term outcomes. Anterior resection for rectal tumors was the most common surgery (44%) but only 93 (15%) of patients underwent laparoscopic colorectal resection associated with a major hepatectomy, confirming the data from Southampton meeting [9] that this type of procedure can be performed only in specialized center. laparoscopic colorectal resection associated with a parenchymal sparing hepatectomy was the most common procedure (85%) and can explain the low conversion rate (2.7%), the operative time (320 min), the estimated blood loss (250 ml), the low morbidity and mortality (0.8%). The availability of experienced hepatobiliary, colorectal surgeons and multidisciplinary team is indispensable for providing the best treatment options possible for

each patient. [9,32-35]

One of the limits of this review is the heterogeneity of the date regarding neoadjuvant chemotherapy, surgical oncology outcome, disease recurrence and overall survival. Interestingly only half of the studies [11,13,15-19,22,23,25,29] reported the use of neoadjuvant chemotherapy, from these only 88 (28%) patients underwent neoadjuvant chemotherapy prior to surgery despite the bad prognostic factors of these patients including, synchronous liver disease, metastatic lymph node (72%), two or more liver metastases (38%) and median largest liver metastases of 54mm [6]. Unfortunately, there is no explanation for the low use of neoadjuvant chemotherapy despite the recommendations. Other limits of this retrospective analysis were missing data regarding number of lymph node harvested during colon resection and the R0 status of liver resection which can limit the assessment quality of the surgical procedure. In addition to the good short-term outcomes, many authors marked the advantages of laparoscopic surgery in general, such as rapid recovery, smaller incision, less pain, less infection, less pulmonary complications and more patient satisfaction. [13]. One of the most important advantages of the one-stage surgical approach is the rapid start of adjuvant treatment which can help in the control of disease recurrence but again this data is missing in most of the reviewed studies.

Conclusion

Simultaneous laparoscopic resection for CRC patients with SLMs can be done safely with minor morbidity and short-term mortality. It can be performed for both major and minor liver resection despite the location of primary CRC for highly selected cases by well-trained HPB and colorectal surgeons after multidisciplinary discussion. This approach can reduce the hospital stay, post-operative infections in addition to the all benefits of laparoscopic surgery. One-Stage laparoscopic surgery gives the advantage of faster application of adjuvant therapy. Randomized controlled multi-centric trials should be conducted in order to adopt this approach as gold standard.

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