Systematic Review

Systematic Review Comparing the Effectiveness of Robotic verse Laparoscopic Liver Surgery in Colorectal Liver Metastasis (CRLM)

Nabeel Merali [1,*], Hajra Ashraf [2], Tarak Chouari [2], Badriya Al Araimi [3], Rajiv Lahiri [1], Timothy A. Rockall [1] and Adam E. Frampton [1]

[1] The Minimal Access Therapy Training Unit, University of Surrey, Daphne Jackson Road, Guildford, Surrey GU2 7XH, UK; rajiv.lahiri@nhs.net (R.L.); t.rockall@nhs.net (T.A.R.); aframpton@nhs.net (A.E.F.)

[2] Croydon University Hospital, London CR7 7YE, UK; ashrafhajra@gmail.com (H.A.); t.chouari@nhs.net (T.C.)

[3] Armed Forces Hospital, Muscat 112, Oman; badria77@gmail.com

* Correspondence: nabeel.merali@gmail.com

Abstract: Introduction: Colorectal cancer (CRC) is the third most common cancer in the world. The liver is the most common site of metastasis with 15 to 25% of patients presenting with synchronous colorectal liver metastasis (CRLM). This study is aimed at evaluating the long- and short-term outcomes of laparoscopic and robotic CRLM surgery, and directly comparing their respective effectiveness. Methodology: A literature search was performed and all studies that reported on operative characteristics, oncological outcomes for CRLM, morbidity or mortality and cost-effectiveness on robotic or laparoscopic surgery were included. The study design was in keeping with the PRISMA guidelines. Results: From the initial 606 manuscripts identified, 19 studies were included in the final qualitative analysis. A total of 1340 patients with 1194 LLR (Laparoscopic Liver Resection) and 146 RLR (Robotic Liver Resection) cases were analysed. Within the LLR group, the average tumour size excised was 32.1 mm compared to the RLR group of 33.8 mm. The average operative time in the LLR was 193 min, CI of 95% (147.4 min to 238.6 min) compared to RLR 257 min, CI of 95% (201.5 min to 313.8 min) with a *p*-value < 0.0001. Estimated blood loss was lower in the RLR group (210 mL) compared with the LLR group (246 mL). Conclusion: Despite the higher operative cost, RLRs do not result in statistically better treatment outcomes, with the exception of lower estimated blood loss and excision of larger CRLMs. Operative time and total complication rate are significantly more favourable with LLRs. Our study has shown that robotic liver surgery is safe and feasible in well-selected patients.

Keywords: colorectal cancer; liver metastasis; oncology; surgery and education

1. Introduction

Colorectal cancer (CRC) is the third most common cancer worldwide [1]. According to Cancer Research UK, bowel cancer is the 4th most common cancer in the UK, accounting for 12% of all new cancer cases. There are around 42,000 new bowel cancer diagnoses in the UK every year, and it is responsible for approximately 8900 deaths annually [2]. The prognosis of colorectal cancer patients is in a large part determined by the presence of metastases. The liver is usually the first site of metastatic disease and may be the only site in 30–40% of patients with advanced disease [3]. Median survival without treatment is <1 year after disease presentation, and with a 5-year survival rate of 13% or less [4]. Safe and effective surgical procedures for treating colorectal cancer patients with liver metastases (CRCLM) have shifted from palliation to prolongation of survival and cure. Surgery is the only treatment that offers the prospect of a cure for CRLMs. In 1993, Woisetschläger R. performed the first laparoscopic CRLM [5]. Over the past decade, there is increasing evidence that laparoscopic liver resection (LLR) has been shown to be feasible and safe [5,6].

Benefits include reduced post-operative pain and ileus, shorter length of stay, rapid return to pre-operative activity and better cosmetic results. The criteria now used for measuring resect-ability are based on whether a macroscopically and microscopically complete (R0) resection of the liver can be achieved, and whether the volume of the liver remaining after resection will be adequate. Figure 1 below outlines the current R classification system nationally used, outlined by the United Kingdom Royal College of Pathologists.
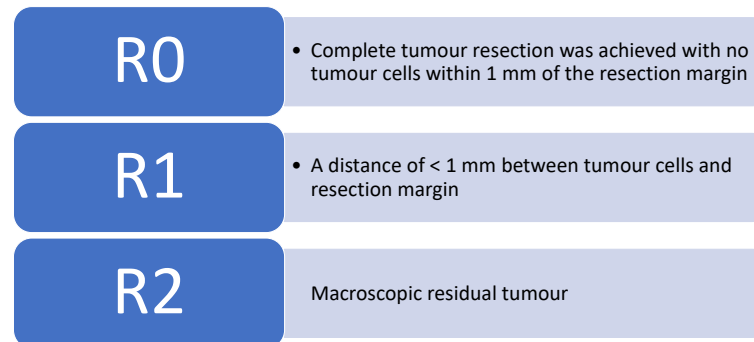
R0
- Complete tumour resection was achieved with no tumour cells within 1 mm of the resection margin

R1
- A distance of < 1 mm between tumour cells and resection margin

R2
Macroscopic residual tumour

Figure 1. The United Kingdom Royal College of Pathologists has stated the current R classification [7].

The emergence of minimally invasive surgery for liver resection has flourished with the introduction of inventive technologies such as fibre optic imaging and ultrasonic haemo-static agents. In addition, growing evidence demonstrates that oncologic results are similar to open surgery in terms of R0 and R1 resections and overall 5-year survival. Operative results and postoperative variables were analysed by minor and major hepatectomy (e.g., more than two segments, right hepatectomy, or left hepatectomy) where appropriate. This study aimed to evaluate the short and long-term outcomes and directly compare the effectiveness of laparoscopic and robotic CRLM surgery.

2. Materials and Methods

The present study was designed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. An electronic literature search of the databases (PubMed/MEDLINE, EMBASE and Cochrane database) in the English language was conducted in February 2020.

The following search terms were used:

- Robotic Surgery AND ((Colorectal Liver Metastasis OR (CRLM))—25
- Laparoscopic surgery AND ((Colorectal Liver Metastasis OR (CRLM))—269
- Liver resection AND ((Colorectal Liver Metastasis OR (CRLM)) AND Robotic Surgery—21
- Liver resection AND ((Colorectal Liver Metastasis OR (CRLM)) AND Laparoscopic surgery—249
- ((COLORECTAL LIVER METASTASIS) OR (CRLM)) AND (("robotic liver surgery" OR ("liver surgery") OR (ROBOT ASSISTED SURGERY) OR (LAPAROSCOPIC SURGERY)) AND ((COST EFFECTIVENESS ANALYSIS) OR (cost effective))—26

Study Design: All titles and abstracts were screened for review with careful examination of the data to remove double counting of patients between series. A total of 19 articles were transferred to Mendeley© reference manager (Elsevier Inc., New York, USA) for full-text review based on the following inclusion criteria.

- That all studies were appropriate prospective and retrospective studies specifically addressing outcomes of patients with CRLM who underwent either laparoscopic or robotics resection.
- Studies that reported on perioperative characteristics, at least one postoperative outcome and oncological outcomes for CRLM, morbidity or mortality and cost-effectiveness on robotic or laparoscopic surgery were included.

The exclusion criteria included studies in which it was impossible to extract data specifically related to CRLM, review articles, editorials, case reports and letters. As well as nonhuman studies and those articles not translated into the English language.

Data Extraction and Statistical Analysis: Two reviewers conducted the literature search and data extraction. Any disagreement was resolved by consensus. Once the search was complete and the studies filtered, data were extracted from each study and analysed into a spreadsheet. Studies were then assessed for common themes which linked them together allowing for the identification of subgroups to allow for systematic review. We excluded results with insufficient data and reports with obvious errors. The PRISMA Flow diagram schematically depicts article selection (Figure 2).
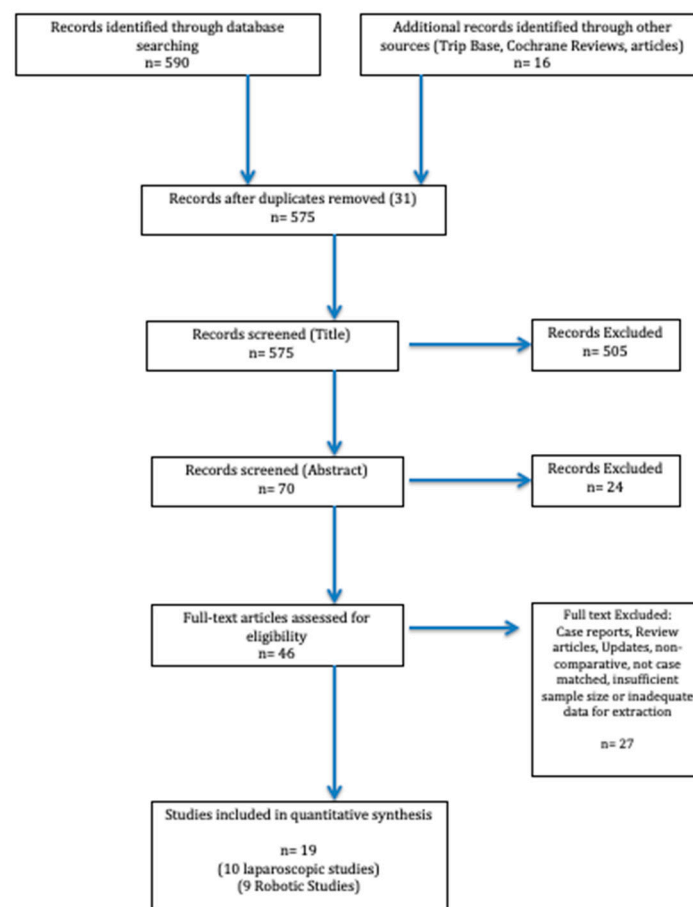
Figure 2. PRISMA flow diagram illustrating the article selection process for the systematic review. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis.

3. Results

The PubMed/MEDLINE, EMBASE and Cochrane database search identified a total of 606 studies. After excluding duplicates and following the PRISMA Guidelines, two independent reviewers carefully reviewed 70 abstracts. A total of 46 studies were identified that were meticulously appraised. In total, 28 articles were excluded according to the inclusion criteria, leaving 19 studies (10 laparoscopic, 9 robotic) that were included in our analysis. A total of 1340 patients with 1194 LLR (Laparoscopic Liver Resection) and 146 RLR (Robotic Liver Resection) cases were analysed. An overview of the reviewed articles and their respective intervention, management strategies and outcomes are highlighted in Tables 1 and 2.

Table 1. Outcomes of the Laparoscopic Liver Resections for CRLM.

Article	Yue et al., 2018	J. Shim et al., 2018	A. Fretland et al., 2018	T. Nomi et al., 2016	S. Ferretii et al., 2015	R. Montalti et al., 2014	S. Schiffman et al., 2014	B. Topal et. al. 2012	H. Topal et al., 2012	A. Hilal 2012
Type of study	Retrospective	Retrospective	Randomised control trial	Retrospective	Retrospective	Retrospective	Retrospective, case series	Retrospective	Prospective study	retrospective, single centre
No. of Cases	241	22	129	120	142	114	242	81	20	83
Age (years)	67 (60–69) & 74 (70–78) NB: Two Age Groups	65.6	67	61	66	66.4	60.8	64.3	57.6	66 (32–85)
Preoperative systemic chemotherapy	187	21	77	71	25	78	128	55	15	Not mentioned
Type of liver resection	18 Major (Left lateral sectionectomy), 223 Minor (wedge/ sectionectomy)	2 Major, 20 Minor	Not mentioned	83 Major cases	39 Major cases, 103 Minor cases	8 major cases, Postero-superior resections 52 (45.6%)	104 major cases, 133 minor cases	18 Major, 34 Minor	20 Major	Major 27, Minor 56
Tumour Size	30 mm (10–50) & 20 mm (10–40)	16 mm (6–101)	Not mentioned	33 mm (5–170)	28 mm (2–100)	40.8 mm ± 2.9	31 mm	>50 mm—7 cases	40 mm (4–70)	25 mm (5–105)
No. of CRLM	2 (1–4)	1 (1–2)	1.5	2 (1–8)	1 (1–9)	1.7	1.37	2	2 (1–6)	1 lesion (54 cases), 2 lesions (21 cases), >3 lesions (8 cases)
CRLM	Not mentioned	14 synchronous, 8 Metachronous	77 Synchronous	67 synchronous	142 synchronous	54 synchronous	Not mentioned	Metachronous 45, synchronous 36	3 synchronous resection	not mentioned
Duration of surgery (min)	190 (150–290) & 180 (160–260)	135 (40–360)	123 (108–138)	245 (60–540)	120 (15–600)	276 ± 10.1	248.7	120 (80–200)	257.5 (75–360)	220 min (40–540)
conversion rate (lap to open)	8 cases	Not mentioned	9 cases	8 cases (6.7%)	7 cases	17 cases	Not mentioned	6 cases	Not mentioned	5 cases
estimated blood loss median (range)	240 (160–410) & 260 (180–430)	100 (30–950)	300 (224–375)	200 (0–3000)	200 (0–1800)	250 (0–2800)	262.5 mL	50 (10–300)	550 (100–4000)	300 (20–3000)
Pringle maneuver use	Not mentioned	22 cases	Not mentioned	Yes performed, pringle time median range: 25 (8–75)	17 cases	12 (10.5%)	Not mentioned	Not mentioned	4 cases	Yes performed for all cases
Resection margin size, R1, etc.	(R0 = 241/R1 = 0/ R2 = 0)	Not mentioned	<1 mm (29 cases), >1 mm (92 cases), involved (8 cases), missed (4 cases)	R0 resection = 113 cases (94.2%)	postive surgical margins = 10 cases	R1 < 1 mm = 14 cases, R0 = 100 cases	R1 Margin positivity 5.5 % = 12 Cases	Not mentioned	R1—1 Case, R0 = 19 Cases with median tumour free margin of 7.5 mm (0–20)	R0—80 Cases (97%) R1—3 cases
RO resection % per cases (LLR)	240/240	N/A	121/129	113/120	132/142	100/114	230/242	N/A	19/20	80/83

Table 1. *Cont.*

Article	Yue et al., 2018	J. Shim et al., 2018	A. Fretland et al., 2018	T. Nomi et al., 2016	S. Ferretii et al., 2015	R. Montalti et al., 2014	S. Schiffman et al., 2014	B. Topal et. al. 2012	H. Topal et al., 2012	A. Hilal 2012
Length of hospital stay	9 (7–23) & 10 (7–32)	8.5 (5–22)	2.3 days (1.8–3)	7 (4–42)	8 (3–84)	6.0 days ± 0.28	6.5 days	5 days (3–7)	8 (5–51)	5 (2–12)
readmission rate within 30 days	Not Mentioned	0	13 cases	Not Mentioned	Not Mentioned	Not Mentioned	Not Mentioned	0	0 cases	0
Re admission Operation rate within 30 days	Not Mentioned	0	5 cases	Not Mentioned	11	6 cases	Not Mentioned	0	0 cases	Not specifically mentioned for CRLMs, however 5 cases returned to theatre
Complication %	30	9	18	41	31	20	20	14	35	11
No. of Complications	73 cases, Not specified	2 cases	24 cases	50 cases (39 liver specific), overall 21 of 50 cases were major complications	44 cases,	23 cases	48 cases (12.8% Liver specific)	11 cases	7 cases	9 major complications (11%)
Type of complication										major
Clavien-Dindo system Grade (G1–5)	Not mentioned	Grade 1 (2 cases)	Not mentioned	G5 = 1	G1 = 2, G2 = 14, G3 = 20, G4 = 5, G5 = 3	Not mentioned	G5 = 1	Not mentioned	Not mentioned	not mentioned
SSI			n/a		0	7	n/a	0	n/a	0
Bleeding	n/a	0	4	2	3	10	n/a	2	1	5
Liver abscess	n/a	0	2	n/a	0	n/a	n/a	1	0	2
Biliary Leakage	n/a	0	1	20	6	n/a	n/a	0	0	2
Liver insufficiency	n/a	0	1	12	1	n/a	n/a	1	1	0
DVC Sepsis	n/a	0	0	n/a	0	n/a	n/a	1	1	0
colorectal leaakge	n/a	1	0	n/a	8	n/a	n/a	0	1	0
Pulmonary/Cardiac	n/a	0	6	4	8	n/a	n/a	0	1	0
MOF (Perionitis)	n/a	0	3	8	1	n/a	n/a	1	1	0
Death	n/a	0	0	1	3	n/a	1	0	0	0

Table 1. *Cont.*

Article	Yue et al., 2018	J. Shim et al., 2018	A. Fretland et al., 2018	T. Nomi et al., 2016	S. Ferretii et al., 2015	R. Montalti et al., 2014	S. Schiffman et al., 2014	B. Topal et. al. 2012	H. Topal et al., 2012	A. Hilal 2012
90-days mortality rate and Estimated DFS/OS	2 cases = 1 case in the elderly group due to liver failure and 1 case in Middle age group due to metastasis to CNS. FU at 34 months in elderly group = 32 deaths (29 reoccurence of disease), Middle age group = 53 deaths (48 reoccurence)	0	Not mentioned	one case, study showed that OS and RFS were acceptable in patients with CRLMs (5 cm). Furthermore, multivariate analysis did not identify the tumor size as a prognostic factor	3 deaths within 30 day mortalitiy Median FU of 29 (1–108 months), 40 patients developed tumour reoccurence	66 (57.9 %) of the cases reoccurence of disease in 30 month follow up R1 margins were significantly related to lower RFS survival ($p = 0.038$) but did not affect OS.	1 death—massive bleed from portal vein	Not mentioned	The estimated DFS and OS rates in the LMLR group at 1, 2, and 5 years were 60, 49, and 43 and 90, 80, and 48% respectively	22 months FU 2 Year DFS/OS 64%/80%
Cost (might not be directly stated)	Not Mentioned	In conclusion, no significant differences in postoperative outcomes were observed between LSLR and OSLR except length of hospital stay, the number of liver metastasis, and the resection margin.	cost difference from open surgery is $94,000	study suggests that LLR for large CRLMs can be performed safely with acceptable long-term outcomes in selected patients. Therefore, tumor size of CRLM should not interfere when selecting the surgical approach	Not Mentioned	Not Mentioned	Not Mentioned	Not mentioned	Not Mentioned	Overall, our data including a large proportion of major hepatectomies confirm the well-established advantages of laparoscopic liver surgery in terms of reduced high-dependency unit and postoperative length of stay.

Table 2. Outcomes of the Robotic Liver Resections for CRLM.

Article	R. Beard et al.2020	S. Guadagni et al., 2019	F. Guerra et al., 2018	R. Dwyer et al., 2018	A. Tsung et al., 2014	Eric C.H. Lai et al., 2011	P.C. Giulianotti et al., 2011	L. Casciola et al., 2011	E. Berber et al., 2010
Type of Study	retrospective multicentre	Retrospective	retrospective multicentre	retrospective single centre	Retrospective Single centre	Retrospective	retrospective, 2 different centers by a single surgeon.	Prospective series single study	retrospective single centre, 9 robotic cases (4 for CRLM)
No. of Patients	115	20 robotic assisted	59 (USS guided Robotic)	6	21	6 Robtic assisted	16	14 Robotic assited LHR	4
Age (years)	61	66	64	59.3	58.4	68.2	57	66.4	68.6
Preoperative systemic chemotherapy cases	63 (54.8%)	12	14 (17%)	6	Not mentioned	Not mentioned	not mentioned	not mentioned	not mentioned
Type of liver resection	18 Minor, 97 Major	20 Major, (3 simultaneous)	39 major, 43 minor	1 Major, 3 Minor, 1 ablation (large segement 7 near vascular structures), 1 no identifiable lesion	16 minor, 4 major	6 Major (3 wedge resections, 3 left lateral sectionectomy)	4 minor (<3 segments) and 12 major resections	14 minor resections, 11 simultaneous procedures	4 minor (peripheral segments)
Tumour Size	25 mm (3 mm–122 mm)	30 mm ± (18)	27 mm (4–130)	Not mentioned	Minor—31 mm (20–55), Major—37 mm (24.5–50 mm)	33 mm ± (16)	47 mm (range, 12–110)	not mentioned	32 ± 13 mm
No. of Metastasis median (range)	1 metastasis = 78 (67.8%), 2 metastasis = 24 (20.9%), >3 metastasis = 13 (11.3%)	2 (2–4)	27 patients had multiple leisons	2	1 (1–2)	Not mentioned	not mentioned	not mentioned	not mentioned
CRLM	49 synchronous cases	6 synchronous cases	16 synchronous	6 (Liver first approach)	not mentioned	9 metachronous, 5 synchronous	not mentioned	3 metachronous, 11 synchronous	not mentioned
Duration of surgery (min)	272 ± 115	198.5 ± (98)	210 min (50–600)	401 (349–506)	253 min (180–355)	190.2 ± 91.6	270 min (range, 90–660)	280 ± 115 min,	258.5 ± 27.9 min
Conversion rate (robotic to open)	6 (5.2%)	0	7 cases (12%)	0	4 cases	0	4 cases	1 case	1 case
estimated blood loss median (range)	Not mentioned	250 (200–300)	200ml (0–1500)	316 (150–1000)	200 (50–337.5)	75 (20–200)	262 mL (range, 20–2000)	245 ± 254 (0–1000)	136 ± 61 mL
Pringle maneuver use	Used at the discretion of the surgeon	Not mentioned	18 cases (30%) during parenchymal transection	Not mentioned	not mentioned	3 cases, Mean time 46.7 min	0	12 cases, mean clamp time 68.9 ± 31.7	not mentioned

Table 2. *Cont.*

Article	R. Beard et al.2020	S. Guadagni et al., 2019	F. Guerra et al., 2018	R. Dwyer et al., 2018	A. Tsung et al., 2014	Eric C.H. Lai et al., 2011	P.C. Giulianotti et al., 2011	L. Casciola et al., 2011	E. Berber et al., 2010
Resection margin size, R1, etc.	R0 = 84 (73.7%), R1 = 19 (16.7%)	R0—20 cases (100%)	R0 resection— 54 cases (92%), R1—5 cases	R0 resection—100%	R0 negative margin—95 % of cases	RO—5 cases, R1—1 case	mean surgical resection margin 25 mm (range, 5–70).	not mentioned	resection margin 11 mm, Resectionmargins were negative for a tumour at the time of resection.
No. of R0 resection per cases	84/115	20/20	27/29	6/6	20/21	5/6	n/a	n/a	4/4
Length of hospital stay	5 (3–6)	4.7 ± 1.8 day	6.7 ± 6.2 days	4.5 (3–10)	4.0 (3.0–5.5)	6.8 mean day ± 2.8	7 days median (2–26)	6.8 ± 2.8 days, NB for synchronous CRLM it was 9 ± 2.6 days	not mentioned
readmission rate within 30 days	8 (7.0%)	0	Not mentioned	0	0	0	not mentioned	0	0
Re admission Operation rate within 30 days	1 (0.9%)	0	1	0	1	1	not mentioned	1	not mentioned
Complication %	10.4	25	27	67	52	16	not mentioned	28	11
No. of Complications	12	5 cases	16 cases (27%)	4 Cases	11 cases	1 case	not mentioned	4 cases	11% of the robotic (mixed result)
Type of complication (Claven-Dindo) Grade (G1–5)	G3 = 12 cases	G1—1 case, G2—4 cases	G1–2 (13 cases, 22%), G3–4 (3 cases 5%)	Not mentioned	G3–4—one case	G2 (1 case)	unable to distinguish complications from other cases (heterogenous data)	4 cases, unable to distinguish complications from other cases (heterogenous data)	unable to distinguish complications from other cases (heterogenous data)
SSI	n/a	n/a	n/a	1	n/a	0	n/a	n/a	n/a
Bleeding	3	n/a	3	0	n/a	0	n/a	2	1
Liver/Intraabdominal abscess/collection	7	n/a	n/a	2 pelvic	n/a	0	n/a	n/a	n/a
Biliary Leakage	n/a	n/a	1	0	n/a	1	n/a	1	n/a
Liver insufficiency	n/a	n/a	n/a	0	n/a	0	n/a	n/a	n/a
DVC Sepsis	n/a	n/a	n/a	0	n/a	0	n/a	n/a	n/a
colorectal leaakge	n/a	n/a	n/a	1	n/a	0	n/a	1	n/a
Pulmonary/Cardiac	n/a	n/a	2	0	n/a	0	n/a	n/a	n/a
MOF (Perionitis)	n/a	n/a	n/a	0	n/a	0	n/a	n/a	n/a
Death	1	n/a	0	0	n/a	0	n/a	n/a	n/a
Other	5	n/a	n/a	n/a		n/a	n/a	n/a	n/a

Table 2. *Cont.*

Article	R. Beard et al.2020	S. Guadagni et al., 2019	F. Guerra et al., 2018	R. Dwyer et al., 2018	A. Tsung et al., 2014	Eric C.H. Lai et al., 2011	P.C. Giulianotti et al., 2011	L. Casciola et al., 2011	E. Berber et al., 2010
90-days mortality rate and Estimated DFS/OS	60 patients (52.2%) had recurrence of their metastatic colorectal cancer following liver resection	FU 22.5 Months, 0 cases of local recurrence 1 Year DFS—89.5%, 3 Year DFS—35.8%	FU 19.5 months—9 disease deaths, 16 cases recurrent disease 1 Year DFS/OS 83.5%/90.4%, 3 Year DFS/OS 41.9%/66.1%	0 Not mentioned	0 NB: Unable to extract true data of CRLM from robotic arm (heterogenous data)	0 1 Year DFS/OS 85%/96%, 3 Year DFS/OS 47%/67%	0 NB: Unable to extract true data of CRLM from robotic arm (heterogenous data)	FU 25.1 ± 11.7 months, two deaths—reoccurence of disease NB: Unable to extract true data of CRLM from robotic arm (heterogenous data)	0 Not mentioned
Cost (might not be directly stated)	accurate data on cost that would allow for a comparison between the RLR and LLR groups are not available.	In our experience, RAS for CRLM surgical treatment was feasible and played a positive role even in patients with multiple metastases and previous or synchronous surgery. RAS seemed to be oncologically effective in this setting, as no patients experienced local relapse in the treated area.	Robotic surgery as a valid option to resect CRLMs competently in terms of both surgical and oncological outcomes.	All were performed without the need for conversion, thus supporting efficacy. The role of robotic surgery in the management	Although a greater proportion of robotic cases were completed in a totally minimally invasive manner, there were no significant benefits over laparoscopic techniques in operative outcomes.	The main drawback of advanced robotic surgery is the associated cost. At the current stage of development, the benefits of robot-assisted surgery in liver surgery have not yet been defined.	This preliminary experience shows that robotic surgery can be used safely for liver resections with a limited conversion rate, blood loss, and postoperative morbidity.	Finally, results of this series show that robot-assisted LHR is safe and feasible and provide considerable evidence that robotics could overcome limitations of traditional LHR associated with tumor location, supporting robot use only for complex resections.	The additional cost incurred by the robot is a concern when justifying its use. Although a case-by-case cost analysis was not done, the robotic instrumentation in general adds $500 per case to the laparoscopic equipment cost.

Pre-operative: The average age in the LLR was 65 years compared to 63 years in the RLR. Within the LLR group, the average tumour size excised was smaller at 32.1 mm compared to the RLR group of 33.8 mm. Preoperative systemic chemotherapy was administered in all of the laparoscopic studies, except one. Major hepatectomies were defined as resection of three or more segments and synchronous metastases were defined as cases in which patients received a diagnosis of CRLM at the same time or within 6 months of the diagnosis of the primary tumour.

Intra-Operative: The operative time was reported in all of the included studies. The data show that the operative time was longer in the RLR group compared with the LLR group. The average operative time in the LLR is 193 min, CI of 95% (147.4 min to 238.6 min) compared to RLR 257 min, CI of 95% (201.5 min to 313.8 min) with a *p*-value < 0.0001. Estimated blood loss was lower in the RLR group (210 mL) compared with the LLR group (246 mL). The need for conversion was similar between individual studies and the majority of the studies did not directly comment on the use of the Pringle Manoeuvre.

Post-Operative: Oncological outcomes were mentioned in 16 studies (9 Laparoscopic, 7 Robotic), concluding high rates of successful R0 margins, independent of the modality of surgery. A total of 1035 from 1090 (95%) patients had an R0 resection margin within the LLR group compared to 82 from 86 (95%) patients that had an R0 resection margin within the RLR group. However, the sample sizes leading to the conclusions are significantly different, 1090 (LLR group) vs. 86 (RLR group). This may produce inconclusive results, as the statistical power to detect a difference would be low. It is clear more patients are required within the RLR group to form a robust statement. From an oncologic standpoint, local and systemic recurrence rate, recurrence site and 1- and 3-year overall and disease-free survival (DFS) were analysed as shown in Tables 1 and 2.

Cost-Effectiveness Comparison: Overall the length of hospital stay (LOS) was shorter in the RLR group at 5.9 days compared to the LLR group of 6.6 days. Within the RLR group, two studies [8,9] commented on 14 cases as grade 1–2 of the clavien–dindo classification (CDC). The LLR group had two studies [10,11] that commented on 18 cases as grade 1–2 CDC. The RLR group had 4 cases that returned to theatre within 30 days post-operatively (ERCP stenting for bile leak). Within, the LLR group, 22 cases returned to theatre within 30 days post-operatively. Due to the heterogeneity of the data, the majority of studies did not directly comment on the percentages of patients re-operated in each group. The most common complication in both groups was post-operative bleeding. Overall the RLR group had a greater number of complications per case (32%) compared to the LLR group (22.9%).

4. Discussion

Surgical resection is the only curative method for CRLM and an R0 resection margin is the ultimate goal. The use of minimally invasive surgery (MIS) has recently been embraced within resectional HPB surgery. Due to the complexity of hepatic resection, there are key concerns that have to be overcome, such as inadequate margins, tumour seeding, missing small metastasis, air embolism and poor oncological outcomes. This review included reports of 1194 patients who underwent laparoscopic liver resections compared to 146 robotic liver resections for CRLMs. From the statistical findings, within the RLR group, larger tumour size was excised with a longer operative time, whereas the estimated blood loss was less compared to the LLR group. High rates of successful R0 margins, independent of the modality of surgery were noted. The mean LOS was shorter in the RLR group compared to the LLR group. The number of complications per case was greater in the RLR group compared to the LLR group. However, neither result was shown to be statistically significant.

One study on short and long-term outcomes of laparoscopic hepatectomy for colorectal liver metastases in the elderly was published by Yue et al., 2018. LLR were performed in 241 consecutive patients over the age of 60 years old with CRLMs. Based on age, they were divided into subgroups. The elderly group (70 years old and above) had 78 patients with a higher American Society of Anaesthesiologist (ASA) score [12]. There was no significant

difference between groups in regards to operative time, blood loss and postoperative complications and they had equal oncological outcomes. Therefore laparoscopic surgery was shown to be beneficial in elderly patients with CRLMs with good short and long-term survival results. The OSLO-COMET randomised controlled trial conducted by Fretland et al., 2018 was the first of its kind to compare LLR to OLR (Open Liver Resection) for CRLMs. A single-centre, double-blinded study randomised 280 patients into two groups, 133 (LLR) and 147 (OLR). The primary outcome was postoperative complications within 30 days, which was 19% in the LLR compared to high morbidity of 31% in the OLR [6]. The operative time and blood loss were similar in both groups; however, the length of stay (LOS) was shorter in the LLR. Interestingly there was no difference in rates of R0 resection or positive margins within the groups and the cost of LLR was higher. A meta-analysis of 610 patients directly comparing laparoscopic versus open liver resection for metastatic colorectal cancer was conducted by Schiffman et al., 2014. LLR were performed in 242 patients compared to 368 patients who underwent OLR [13]. There was no difference in terms of age, sex, tumour size or number of metastasis in either group. The major findings in this study were decreased estimated blood loss, need for transfusion, LOS and overall complication rates in LLR compared to OLR. In conclusion, it was found that patients were able to tolerate laparoscopic surgery with overall reduced morbidity and good oncological outcome. However, Schiffman stated that patients with multifocal, bilobar tumours, tumours invading the inferior vena cava or confluence junction of portal vein would not be ideal candidates for Minimum Invasive Surgery (MIS). Ferretti et al., 2015 designed a multicentre international study of case series performing simultaneous laparoscopic resection of the primary colorectal cancer and synchronous CRLMs. A total of 142 cases were performed and the median number of liver lesions was 1 (1–9) with an average operative time of 360 (120–690) min [10]. The most important finding was the global morbidity of 31%, lower than comparable open studies. Abu Hilal et al., 2012 conducted a large single-centre study, of 133 laparoscopic liver resections within the UK. A total of 83 cases were CRLMs related and their study demonstrates that the laparoscopic approach is feasible and safe, even when more extreme repeated hepatectomies for recurrent CRLM or 2-stage laparoscopic liver resections for bilobar CRLM are required [14]. An R0 resection margin was obtained in 112 of 116 resections (97%).

It is noted that there are limitations to laparoscopic liver surgery, such as loss of depth perception (stereopsis) in a two-dimensional field, fulcrum effect against ports, a limited degree of movement required for meticulous steps leading to reduced surgical accuracy and tremor intensification. Robotic surgery was developed to overcome many of these limitations. Fundamental features such as instruments that provide better ergonomics with a 7 degree of freedom for movement and tremor filtering, three-dimensional imaging will display deformation of deeper structures and more precise anatomy. Casciola et al., 2011 described the benefits of robotic liver surgery, particularly in resecting lesions in the posterior-superior segments (VII and VIII) as they required curved transections, hepatocaval dissection and bilioenteric reconstruction, which are very challenging with laparoscopy [15]. The surgeon is able to control the camera and instruments simultaneously, eliminating inappropriate camera control or retraction. The presence of computerised console can allow image-guided surgery that is becoming attractive in hepatobiliary surgery [16]. Pesi et al., 2019 analysed surgical and oncological outcomes of a series of 51 patients who received ultrasound-guided robotic liver resections (RLRs) for both primary and secondary malignancies. Their results showed that robotic liver surgery is effective with acceptable uncompromised long-term oncological outcomes [17]. Fruscione et al., 2019 compared robotic-assisted (57 cases) versus laparoscopic (116 cases) major liver resections from a single centre. They concluded that patients who underwent robotic surgery had a lower rate of postoperative ICU admission and lower re-admission rate within 90 days compared to the laparoscopic group [18]. This study has several limitations. The retrospective nature of the study incorporates selection bias. Two surgeons with no evidence of case matching performed all the cases. Purposing that a major hepatectomy

and technically challenging cases (high risk of bleeding or achieving R0 resection) should be performed robotically. Especially as robotic surgery has superior ergonomics and can overcome surgical fatigue delivered by prolonged laparoscopy.

Guerra et al., 2018 published a multi-centre study of 59 patients receiving ultrasound-guided robotic resection for CRLMs. A total of 82 liver resections were performed with a median operative time of 210 min and an estimated blood loss of 200 mL [8]. Overall 7 operations were converted to open surgery, mainly due to uncontrolled bleeding during parenchymal transection. The mean LOS was 6 days and R0 resection was achieved for 92% of lesions. This study illustrates that robotic surgery is effective in resecting CRLMs with similar oncological outcomes to laparoscopic or open surgery. Dwyer et al., 2018 presented a series of synchronous robotic surgery for CRLMs. The retrospective study consisted of 6 patients who underwent colonic resections with an average of 2.25 liver segmentectomy. In all cases, liver surgery was performed first. A mean operative time of 401 min was found, with an estimated blood loss of 316 mL, no conversion to open, LOS of 4.5 days and no 30-day mortality [19]. This small case series illustrates that one-stage synchronous robotic surgery is safe and feasible in well-selected patients. Tsung et al., 2014 published the largest series comparing robotic to laparoscopic liver resections. A total of 57 robotic liver resections were compared to 114 laparoscopic cases. In regards to CRLMs, 21 patients had RLR compared to 36 LLR. There were no significant differences between the operative and postoperative outcomes of robotic and laparoscopic groups. Both had similar oncological margins. However, the robotic group had a significantly greater overall room time (342 vs. 261.5 min, $p < 0.001$) and Operating time (253 vs. 198.5 min, $p = 0.001$) [20]. The likely reason being the additional time required for docking the robot, exchange and repositioning of instruments. A greater number of complex major hepatectomies were performed robotically with a total minimally invasive technique, which would be favorable to patients and many surgeons.

Major hepatectomy or resections in posterior-superior segments have been described to be difficult even in laparoscopic procedures, and these cases theoretically may benefit from robotic surgery. Within our results, Montalti et al., exclusively compare robot-assisted to laparoscopic parenchymal-preserving liver posterior superior resections for lesions located in segments 7, 8, 4a, and 1. Thirty-six patients who underwent RLR were matched with 72 patients undergoing LLR. There were no significant differences in postoperative outcomes as measured by blood loss, hospital stay, R0 negative margin rate, and mortality [21]. Ziogas et al., performed a meta-analysis specifically addressing the comparison between major liver resections performed laparoscopically and robotically [22]. Seven retrospective cohort studies comparing LLR ($n = 300$) versus RLR ($n = 225$) were identified. There was no significant difference observed between the overall complication rates between the two groups. There was no significant difference observed for blood loss, operative time and length of stay. Rahimli et al. compared their robotic and laparoscopic liver surgery for colorectal liver metastases results from a single study centre in Germany. The proportion of major resections was higher in the robotic group with five patients (3 left hemi-hepatectomy, 1 right hemi-hepatectomy, >3 segmental resections). The laparoscopic major resection group consisted of three patients (1 right hemi-hepatectomy, >3 segmental resections, 3 segmental resections). Direct comparison of major resections showed robotic surgery to be longer (412 min in RLR vs. 363.6 min in LLR), less peri-operative blood loss (600 mL in RLR vs. 762.5 ml in LLR) and longer length of stay (12.4 days in RLR vs. 11.5 days in LLR) [23]. There was a trend towards higher R0 resections in the robotic group; this may be related to more precise control of parenchymal dissection.

Daskalak et al., 2017 assessed the clinical outcomes and economic impact of robotic and open liver surgery in a single centre. Within the robotic group, there were 68 robotic cases (29 major, 39 minor) compared to the open group of 55 cases (24 major, 31 minor). An independent company performed the financial analysis comparing six categories of cost (anaesthesiology, operating room, ICU, nursing, pharmacy and re-admission). On average, there was no difference in anaesthetic costs between the two surgery types. It was

noted, however, the mean estimated blood loss, complication rates and overall morbidity were considerably less in the robotic group. The length of stay in the intensive care unit (ICU) was shorter for patients who underwent a robotic procedure (2.1 versus 3.3 days; $p = 0.004$) [24]. The average total cost, including readmissions, was less for the robotic group compared to the open group. Their study illustrated that using the robot for complex cases would lead to an overall reduction in complications, directly impacting on a shorter length of hospital stay and re-admission costs. With time this would become a real cost-benefit, even if the initial intraoperative costs are higher. Bearing in mind this is all supposition and unproven. The key message is remembering the early financial impact of laparoscopic liver resections had when compared to open surgery. Initially, there is higher intraoperative cost and longer operative times, however, a clear benefit in a shorter length of hospital stay and morbidity leading to a reduction in overall hospital costs [25]. Fretland et al., 2018 estimated in a 4-month health care perspective that laparoscopy had a 95,000 USD threshold and was cost-effective compared to open surgery [6]. However, Berber et al., 2010 stated the additional cost gained by robotic instrumentation adds 500 USD per case to the laparoscopic equipment cost [26]. The additional operative time in RLRs compared to LLRs was ascribed to unfamiliarity with the new technology, setup and learning curve.

Several limitations of our study should be mentioned. Firstly, the studies included a small number of patients in the robotic group compared to the laparoscopic group. All data regarding patient demographics, tumour characteristics, intraoperative variables, and postoperative outcomes were retrospectively collected from medical records incorporates selection bias. RLR group studies did not directly state whether docking time was included in the operative time. The heterogeneity of data directly weakens the significance of our statistical results of weighing advantages and disadvantages. Many studies had insufficient information to allow exact criteria matching.

5. Conclusions

Despite the higher operative cost, RLRs do not result in statistically better treatment outcomes, with the exception of lower estimated blood loss and excision of larger CRLMs. Operative time and total complication rate are significantly more favourable with LLRs. Our study has shown that robotic liver surgery is safe and feasible in well-selected patients. Major advantages over laparoscopy are 3D imaging, better ergonomics leading to precise operative dexterity and improved surgical comfort. However, the available evidence on robotic liver surgery is still limited and definitive conclusions on the actual role of robotics cannot be drawn, especially long-term oncological and cost benefits. Furthermore, a well-designed, randomised control study is required to assess the actual advantages of robotic over laparoscopic liver surgery for CRLMs.

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