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Comparing Open, Laparoscopic and Robotic Liver Resection for Metastatic Colorectal Cancer—A Systematic Review and Network Meta-Analysis

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ABSTRACT

Colorectal liver metastases (CRLM) can be surgically managed through open resections (OLR), laparoscopic resections (LLR), or robotic liver resections (RLR). However, there is ongoing uncertainty regarding the safety and effectiveness of minimally invasive approaches like LLR and RLR. This study aims to clarify these issues by conducting a network meta-analysis (NMA) to compare outcomes across OLR, LLR and RLR for patients with CRLM. Following the PRISMA-NMA guidelines, the meta-analysis included 13 studies with a combined total of 6582 patients. Of these, 50.6% underwent LLR, 45.3% underwent OLR, and 4.1% underwent RLR. The analysis found no significant differences in R0 resection rates between LLR (odds ratio [OR] 1.03, 95% confidence interval [CI]: 0.84–1.26) and RLR (OR 1.57, 95% CI: 0.98–2.51) when compared to OLR. Additionally, there were no significant differences in disease-free survival (DFS) and overall survival (OS) at 1, 3, and 5 years. Despite these findings, both LLR and RLR were associated with reduced postoperative complication rates (RLR: OR 0.52, 95% CI: 0.32–0.86; LLR: OR 0.50, 95% CI: 0.37–0.68). However, patients undergoing LLR were more likely to require conversion to open surgery compared to those undergoing RLR (OR: 12.46, 95% CI: 2.64–58.67). Furthermore, RLR was associated with a reduced need for blood transfusions (OR: 0.13, 95% CI: 0.05–0.32), and LLR resulted in shorter hospital stays (mean difference: −6.66 days, 95% CI: −11.6 to −1.88 days). This study demonstrates the oncological safety of LLR and RLR approaches for CRLM relative to OLR, with enhanced perioperative outcomes anticipated following minimally invasive resections of CRLM.

1 | Introduction

Colorectal cancer (CRC) is the 3rd most common diagnosed malignancy worldwide, with the liver being the most common site of metastasis [1, 2]. The management of CRC has evolved in recent times, with enhanced oncological and survival outcomes anticipated for the majority, largely due to an increased understanding of tumour biology underpinning CRC, improved screening detection programs, the centralisation of cancer services, and the novel multimodal systemic treatments deployed to manage the disease [3]. Nevertheless, approximately 20%–30% of patients treated initially with curative intent will develop colorectal liver metastasis (CRLM), and the anticipated 5-year-overall survival (OS) outcomes for those with stage IV disease is 20% [3, 4]. Over the last few decades, refinement of the surgical practice has facilitated the resection of hepatic metastases in the setting of CRC, has translated to improved survival outcomes [3]. Liver resection remains the gold standard of management of CRLM, alongside the prescription of (neo)adjuvant chemotherapy [5, 6]. Importantly, the anticipated survival outcomes for these patients correlate strongly with the extent of hepatic metastases; thus, performing liver resections tends to be reserved for those with oligometastatic disease, with isolated to defined segments of the liver, with patients with more advanced disease often considered 'inoperable' and indicated for palliative treatments [7].

Traditionally, liver resection was performed as an open procedure (OLR), however the recent paradigm has evolved such that minimally invasive surgical (MIS) techniques including laparoscopic liver resection (LLR), and robotic liver resection (RLR) have become widely adopted into clinical practice [8]. There is recent evidence to suggest that MIS may be pragmatic, due to an association with reduced complication rates, shorter length of hospital stay (LOS), and reduced intraoperative blood loss (IOBL) when compared to conventional OLR [9, 10]. Nevertheless, OLR remains the surgical approach of choice for more challenging cases, with some surgical centres lacking accessibility to newer minimally invasive approaches [11, 12].

There is evidence suggesting that similar oncological outcomes may be expected following LLR and OLR for CRLM, particularly in the setting of metastatic liver recurrence [10, 13–15]. More recently, RLR, the first was described by Giulianotti in 2003 [16], with data subsequently indicating that this approach may be advantageous in overcoming some technical limitations experienced in LLR for certain cases, such as higher complete resection rates, increased manual dexterity and increased ergonomics for the surgeon [17–19]. Furthermore, there is a paucity of randomised clinical trials (RCTs) investigating the short- and long-term oncological outcomes following RLR [20, 21], which has rendered it challenging for expert consensus statements to endorse RLR for CRLM, with 6 of the 14 currently available recommendations relying on data from low quality evidence, predominantly experts opinions [22]. Therefore, the aim of the current study is to apply network meta-analysis (NMA) methodology to the available current data to evaluate the oncological safety of MIS for CRLM.

2 | Methods

2.1 | Literature Search

A formal systematic search was performed of the PUBMED, EMBASE, and COCHRANE databases in accordance to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) checklist, incorporating NMAs of healthcare interventions [23]. An initial predefined search strategy was outlined by the senior authors (M.G.D and N.D). Two authors (L.B.M and E.K) conducted independent searches of the four databases to identify studies suitable for inclusion, the latest of which occurred in September 2023. The search terms were as follows: (liver resection), (open), (laparoscopic), (robotic) which were all linked with the Boolean operator 'AND'. Studies were combined from the three databases and duplicate studies were then manually removed. Studies were limited to those published in the English language. Studies were not restricted based on year of publication. Proceedings from academic conferences were excluded. All studies had their titles screened initially and studies considered to be relevant had their abstracts and full texts reviewed.

2.2 | Eligibility Criteria

Studies meeting the following predetermined inclusion criteria were considered for inclusion in this systematic review [1]: studies comparing the outcomes of two or more methods of surgical intervention for CRLM (i.e., OLR, LLR or RLR) [2]; studies had to compare data with respect to oncological (i.e., margin-negative resection [R0]), survival (i.e., OS), or post-operative surgical (e.g., estimated blood loss) outcomes and [3] studies had to provide full-text manuscripts to warrant inclusion.

The exclusion criteria were [1] studies not evaluating the outcomes of surgical interventions for CRLM patients [2]; studies which combined MIS techniques [3]; conference abstracts [4]; review articles [5]; case reports [6]; editorial articles or [7] studies not published in the English language.

2.3 | Data Extraction and Quality Assessment

Data was extracted from the included studies as to follow the predefined outcome measures. Outcome measures were divided into survival, surgical and oncological outcomes. Survival outcomes included 1-year, 3-year and 5-year disease-free survival (DFS) and OS, along with 30-day and 90-day mortality. Surgical outcomes included intraoperative and postoperative outcomes, while oncological outcomes included negative resection margins (R0). Basic clinicopathological parameters were obtained from the studies, including previous liver resections and the incidence of major hepatic resection, defined as resection of four or more liver segments [24]. The evaluation of risk of bias and methodological quality of the included nonrandomised studies adhered to the Newcastle-Ottawa scale [25]. Risk of bias of the included RCTs was assessed using the Jadad scale [26].

2.4 | Statistical Analysis

Descriptive statistics were utilised to delineate the characteristics of the trials included. Data pertaining to recurrence, OS, morbidity, complications, and readmission were presented as binary outcomes, depicted as odds ratios (ORs) with corresponding 95% confidence intervals (CIs). ORs were computed based on raw event data from studies comparing interventions using per-protocol data when applicable. Continuous data were analysed using mean values, standard deviations (SDs), and pooled mean variance, with differences expressed as weighted mean differences (WMDs). Throughout the analyses, OLR served as the primary comparator. NMAs were carried out using the netameta and Shiny packages for R [27, 28]. Effect size point estimates were presented with 95% CIs, with results deemed of significance when $p < 0.050$ level, or if the 95% CI did not encompass a value of 1. Mean and SD estimates were computed employing standard statistical methodologies when appropriate [29, 30].

Rank probabilities were graphed against possible ranks for all treatment options under consideration. The confidence in outcome estimates was evaluated using the Confidence in Network Meta-Analysis (CINeMA) tool [31].

3 | Results

3.1 | Literature Search

The literature search yielded a total of 1165 studies. Following the removal of 264 duplicate studies, 901 independent studies had their titles screened for relevance for inclusion in this study. Of these, 142 had their abstracts reviewed for relevance and 49 required full text manuscript review. Overall, 13 studies were included in this systematic review [15, 32–43]. A PRISMA flow diagram detailing the systematic search process is outlined in Figure 1.

3.2 | Study Characteristics

A total of 6582 patients with CRC were included, of whom 3333 underwent LLR (50.6%, 3333/6582), 2,981 underwent OLR (45.3%, 2981/6582) and 268 patients underwent RLR (4.1%, 268/6582). Of the 13 included studies, two were RCTs [34, 37], 1 was of prospective, nonrandomised design [33], and the remaining 10 were of retrospective design [15, 32, 35–36, 38–43]. Furthermore, 4 of the 13 included studies were of multicentre design [38–41]. Basic study characteristics and clinical parameters are highlighted in Table 1.

3.3 | Clinicopathological Data

In total, 60.1% of included patients were male (3887/6407—12 studies). The mean age at diagnosis was 63.4 years (range: 26–93 years) (13 studies). The mean body mass index (BMI) of

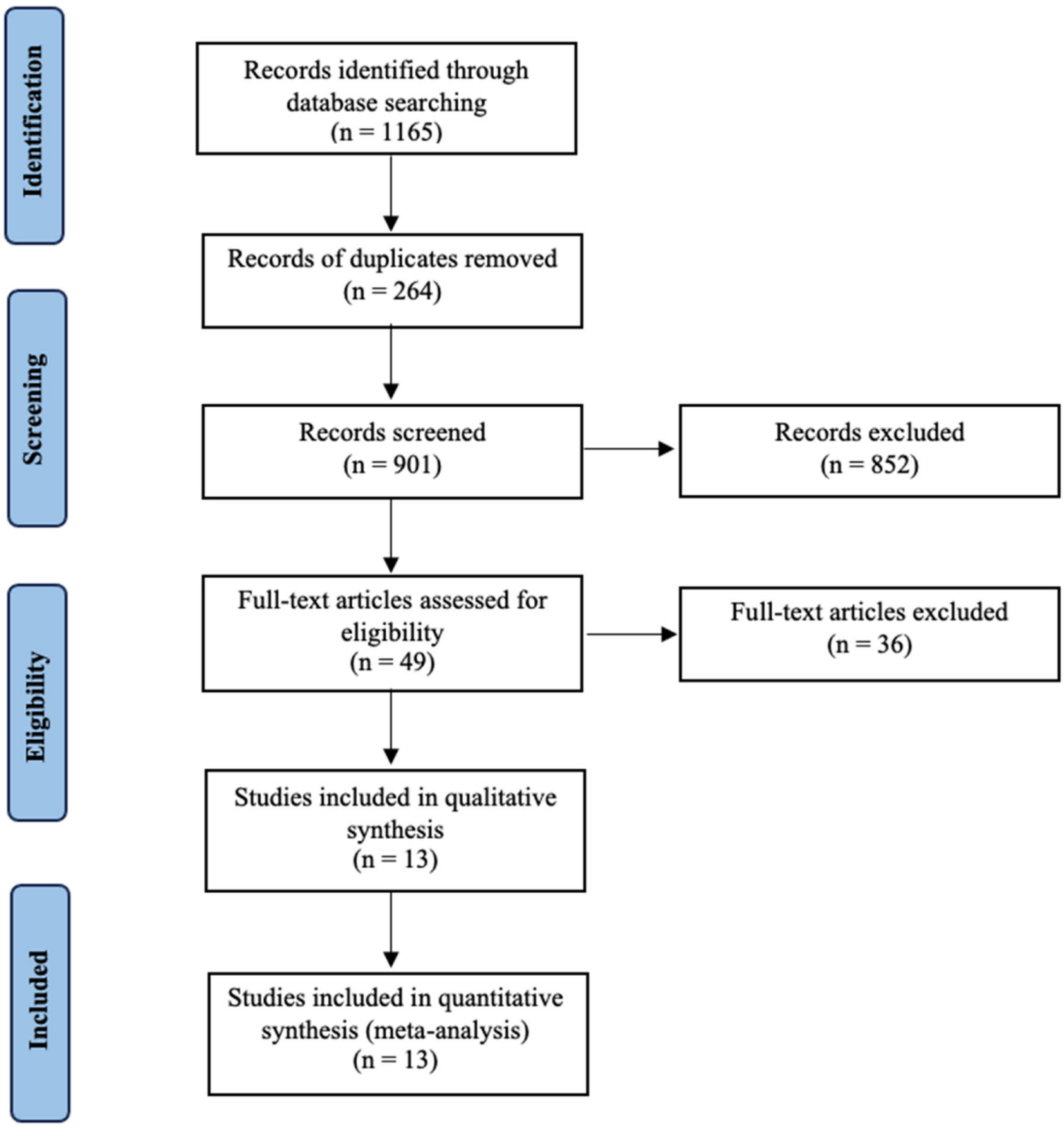

FIGURE 1 | PRISMA flow diagram detailing the systematic search process.

TABLE 1 | Included studies and basic clinical parameters.

Author	Year	Country	Multicentre	LOE	Surgery	N	M/F	Age	BMI	NOS Score	Jadad Score
Cannon	2012	US	No	Retrospective	OLR	140	NA	62 ± 11	27 ± 6	7	—
					LLR	35		62 ± 10	28 ± 8		
Guerron	2013	US	No	Prospective	OLR	40	25/15	62.2 ± 1.8	NA	7	—
					LLR	40	19/21	66.2 ± 1.9			
Fretland	2018	Norway	No	RCT	OLR	147	87/60	66 ± 10	25 ± 4	—	3
					LLR	133	77/56	67 ± 8	26 ± 5		
Ratti	2018	Italy	No	Retrospective	OLR	412	231/181	59.3 ± 7.2	NA	8	—
					LLR	104	58/46	60 ± 7.7			
Shim	2018	South Korea	No	Retrospective	OLR	101	67/34	60.1 ± 10.5	23.9 ± 3.5	7	—
					LLR	22	17/5	65.5 ± 8.9	23.7 ± 3.1		
Robles-Campos	2019	Spain	No	RCT	OLR	97	71/26	67.5 ± 3.3	27 ± 0.7	—	3
					LLR	96	61/35	65.5 ± 2.3	27.5 ± 1		
Beard	2020	US	Yes	Retrospective	LLR	115	75/40	61 ± 12	29 ± 6	8	—
					RLR	115	76/39	61 ± 11	28 ± 6		
Rahimli	2020	Germany	No	Retrospective	LLR	13	10/3	62.1 ± 12.6	28.3 ± 7.6	7	—
					RLR	12	6/6	63.5 ± 11.3	26.2 ± 2.7		
Masetti	2021	Italy	Yes	Retrospective	LLR	953	589/364	65.6 ± 10.9	25.6 ± 4	6	—
					RLR	77	50/27	65 ± 10.6	26.3 ± 4		
Cacciaguera	2022	UK	Yes	Retrospective	OLR	1792	1100/692	65 ± 10.2	NA	8	—
					LLR	1595	987/608	65.7 ± 10.9			
Gumbs	2022	France	Yes	Retrospective	OLR	142	76/66	64.4 ± 10.8	29 ± 5.3	8	—
					LLR	142	72/70	64.5 ± 12.4	28.7 ± 4.4		
					RLR	22	6/16	60.4 ± 12.4	27.7 ± 4.9		
Shapera	2023	US	No	Retrospective	OLR	42	6/8	69 ± 12.3	27 ± 6.3	6	—
					RLR	14	26/16	61 ± 13.5	28 ± 5.7		
Rozhkova	2023	Ukraine	No	Retrospective	OLR	96	51/45	60.3 ± 11.3	26 ± 4.1	8	—
					LLR	85	44/41	55.9 ± 10	30.7 ± 4.8		

Abbreviations: BMI, body mass index; F, female; LOE, levels of evidence; M, male; N, number; NOS, Newcastle-Ottawa Scale; UK, United Kingdom; US, United States.

the patients was 27.1 (range: 23.7–29.0) (10 studies). The mean size of the hepatic lesion was 3.7 cm (11 studies). Overall, 13.4% of patients underwent major hepatic resections (333/2477—7 studies). The mean preoperative carcinoembryonic antigen (CEA) levels of 84.0 ng/mL (seven studies). Basic pathological parameters are highlighted in Table 2.

3.4 | Oncological and Survival Outcome Measures

3.4.1 | Oncological Outcome Measures

3.4.1.1 | R0 Resection Rates. Overall, 69.2% of studies reported R0 resection rates (nine studies). The overall R0 resection rate was 84.5% (4999/5918). OLR had the highest R0 resection rate (87.7%, 2277/2597—six studies), followed by LLR (84.6%, 2501/2957—seven studies) and RLR (82.1%, 202/246—four studies). At NMA, OLR demonstrated no significant difference in R0 resection rates following LLR (OR 1.03, CI 0.84–1.26) and following RLR (OR 1.57, CI 0.98–2.51) (Figure 2).

3.4.2 | DFS

Overall, 30.8% of studies reported 1-year and 3-year DFS (four studies), while 38.5% reported 5-year DFS (five studies).

At 1-year, LLR had the most favourable DFS (78.6%, 180/229—four studies), followed by OLR (73.6%, 245/333—three studies) and RLR (41.7%, 5/12—one study). At NMA, OLR demonstrated no significant difference in 1-year DFS relative to LLR (OR 1.65, CI 0.88–3.12) and RLR (OR 0.61, CI 0.10–3.58) (Figure 3a).

Similarly, at 3-years, LLR had the most favourable DFS (41.0%, 94/229—four studies), followed by OLR (39.6%, 132/333– three studies) and RLR (16.7%, 2/12—one study). At NMA, OLR demonstrated no significant difference in 3-year DFS following LLR (OR 1.07, CI 0.74–1.55) and following RLR (OR 0.34, CI 0.05–2.34) (Figure 3b).

At 5-years, OLR had the most favourable DFS (34.5%, 271/785—five studies) followed by LLR (26.7%, 96/360—five studies).

3.4.3 | OS

Overall, 30.8% of studies reported 1-year and 3-year OS (four studies), while 38.5% of studies reported 5-year OS (five studies).

At 1-year, RLR had the most favourable OS (100%, 12/12—one study), followed by OLR (96.4%, 321/333—three studies) and LLR (93.0%, 213/229—four studies). At NMA, OLR demonstrated no significant difference in 1-year OS compared to LLR (OR 0.95, CI 0.35–2.59) or RLR (OR 11.29, CI 0.46–277.37) (Figure 3c).

At 3-years, LLR had the most favourable OS (69.4%, 159/229—four studies) followed by OLR (69.3%, 231/333—three studies) and RLR (41.7%, 5/12—one study). At NMA, OLR demonstrated no significant difference in 3-year OS compared to LLR (OR 0.93, CI 0.63–1.38) or RLR (OR 0.42, CI 0.08–2.17) (Figure 3d).

At 5-years, OLR had the most favourable OS (60.8%, 477/785—five studies), followed by LLR (53.1%, 191/360—five studies). At NMA, OLR demonstrated no significant difference in 5-year OS compared to LLR (OR 1.03, CI 0.77–1.37) (Figure 3e).

3.4.4 | 30- and 90-Day Mortality

Overall, 69.2% of studies reported data on 30-day mortality (nine studies) and 30.8% of studies reported data on 90-day mortality (four studies).

For 30-day mortality, there were 14 reported cases (0.5%, 14/2660). Both RLR (0.7%, 2/268—five studies) and OLR (0.7%, 6/862—six studies) had similar 30-day mortality rates, followed by LLR (0.3%, 5/1530—eight studies). At NMA, OLR demonstrated no significant difference in 30-day mortality rates compared to LLR (OR 1.01, CI 0.29–3.58) or RLR (OR 1.24, CI 0.24–6.36) (Figure 3f).

For 90-day mortality, there were six reported cases (0.8%, 6/767). OLR had the highest 90-day mortality rates (1.4%, 4/296—three studies), followed by RLR (0.6%, 1/179—three studies) and LLR (0.3%, 1/292—three studies). At NMA, OLR demonstrated no significant difference in 90-day mortality rates compared to LLR (OR 0.64, CI 0.08–5.24) or RLR (OR 0.45, CI 0.07–3.03) (Figure 3g).

3.5 | Surgical Outcome Measures

3.5.1 | Intraoperative Outcomes

3.5.1.1 | Intraoperative Duration. Overall, 92.3% of studies reported on intraoperative duration (12 studies). The overall mean intraoperative duration was 221.2 min. LLR had the lowest mean intraoperative duration (191.8 min—10 studies), followed by OLR (204.3 min—nine studies) and RLR (304.1 min—five studies). At NMA, OLR demonstrated no significant difference in intraoperative duration compared to those who underwent LLR (MD: −17.63, CI −39.33–4.07) and in those who underwent RLR (MD 31.00, CI −6.75–68.75) (Figure 4a).

3.5.2 | Intraoperative Complications

Only 15.4% of studies reported data with regard to intraoperative complications (two studies). Overall, 9.2% of patients were reported to have intraoperative complications (28/305). RLR had the highest rate of intraoperative complications (25.0%, 3/12—one study), followed by LLR (11.0%, 16/146—one study) and OLR (6.1%, 9/147—two studies). At NMA, OLR demonstrated no significant difference in intraoperative complications compared to those who underwent LLR (OR 1.66, CI 0.69–4.02) or RLR (OR 0.33, CI 0.01–17.20) (Figure 4b).

TABLE 2 | Basic pathological parameters.

Author	Surgery	*N*	Size of Lesion (cm)	Major Resection	Pre-op CEA levels	Neoadjuvant CTx	Previous abdominal surgery	Previous liver resection	Pringle manoeuvre
Cannon	OLR	140	5 ± 3	NA	77 ± 163	118	NA	NA	NA
	LLR	35	4 ± 3		52 ± 126	31			
Guerron	OLR	40	3.2 ± 0.3	NA	37 ± 20	26	NA	NA	NA
	LLR	40	3.3 ± 0.3		45 ± 20	27			
Fretland	OLR	147	NA	NA	44.3 ± 95.1	NA	NA	13	NA
	LLR	133			68.3 ± 149.1			23	
Ratti	OLR	412	4.3 ± 1.75	111	87.3 ± 45.7	336	NA	75	385
	LLR	104	4.9 ± 1.85	28	169.2 ± 97.8	85		19	91
Shim	OLR	101	3.9 ± 1.9	NA	NA	19	NA	NA	NA
	LLR	22	3.5 ± 2.4			1			
Robles-Campos	OLR	97	3.7 ± 2.3	7	10.3 ± 3.2	32	NA	NA	15
	LLR	96	3.7 ± 1.5	11	12 ± 4.3	27			29
Beard	LLR	115	5.1 ± 2.5	21	NA	56	NA	NA	NA
	RLR	115	4.4 ± 2	18		64			
Rahimli	LLR	13	2.8 ± 1.9	3	40.1 ± 51.8	10	10	NA	NA
	RLR	12	4.2 ± 1.6	5	171.5 ± 404.8	10	11		
Masetti	LLR	953	NA	81	NA	NA	NA	NA	NA
	RLR	77		9					
Cacciaguera	OLR	1792	3.5 ± 4.9	NA	NA	1206	1206	161	691
	LLR	1595	2.8 ± 4.1			1004	562	82	662
Gumbs	OLR	142	2.7 ± 1.3	12	154 ± 86.7	104	91	NA	36
	LLR	142	2.5 ± 1.1	11	266.4 ± 160.3	99	87		38
	RLR	22	2.5 ± 1.1	5	25 ± 8.7	19	12		1
Shapera	OLR	42	4 ± 2.1	NA	NA	NA	7	NA	0
	RLR	14	3 ± 1.9				24		0
Rozhkova	OLR	96	5.5 ± 2.3	8	NA	68	NA	NA	NA
	LLR	85	2.8 ± 0.9	3		55			NA

Abbreviations: CEA, carcinoembryonic antigen; *N*, number.

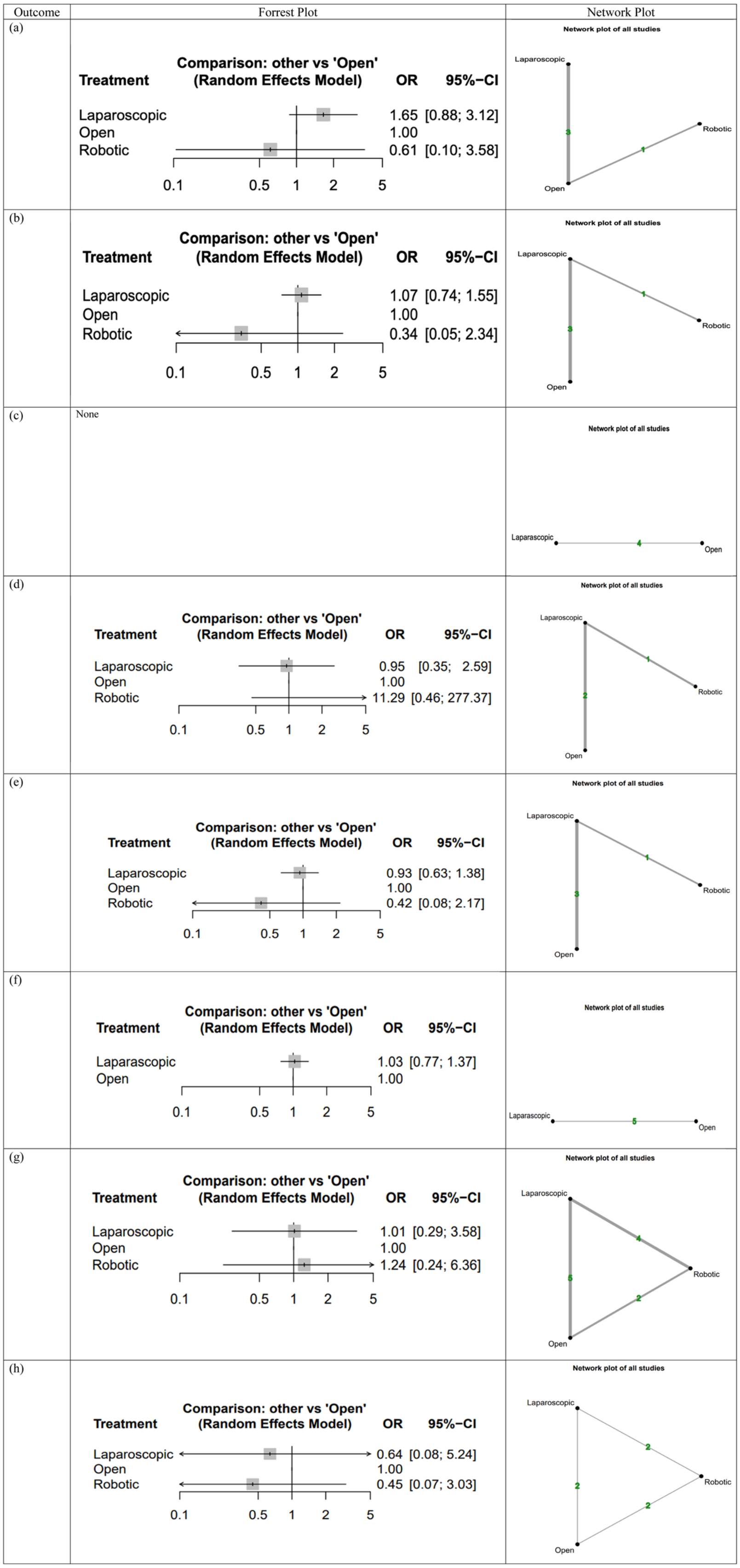

FIGURE 2 | Forrest and network plots with respect to survival outcomes. (a) 1-year DFS; (b) 3-year DFS; (c) 5-year DFS; (d) 1-year OS; (e) 3-year OS; (f) 5-year OS; (g) 30-day mortality and (h) 90-day mortality.

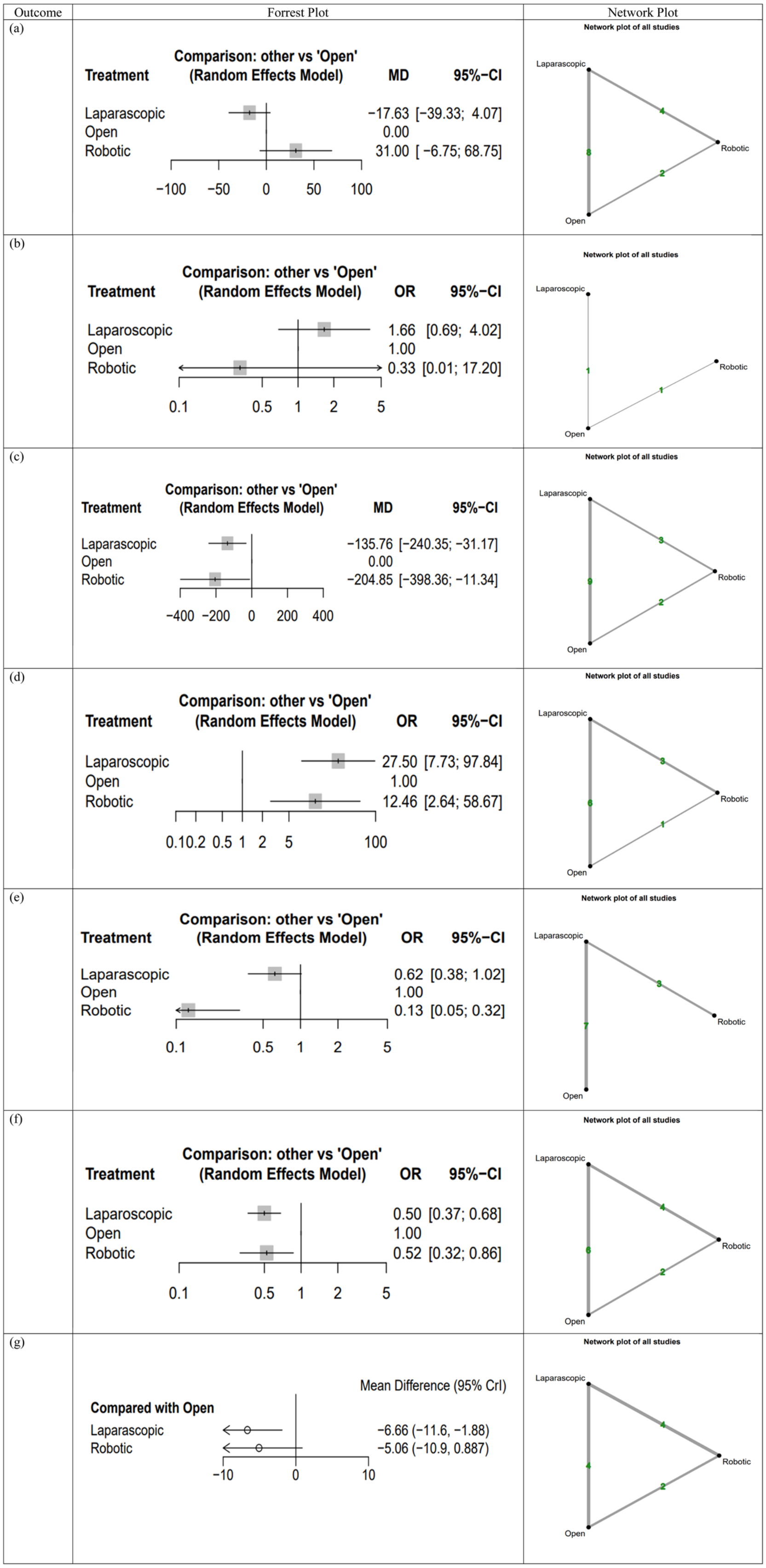

FIGURE 3 | Forrest and network plots with respect to surgical outcomes. (a) Mean intraoperative duration; (b) intraoperative complications; (c) mean intraoperative blood loss; (d) conversion to open; (e) blood transfusion; (f) postoperative complications; and (g) hospital stay.

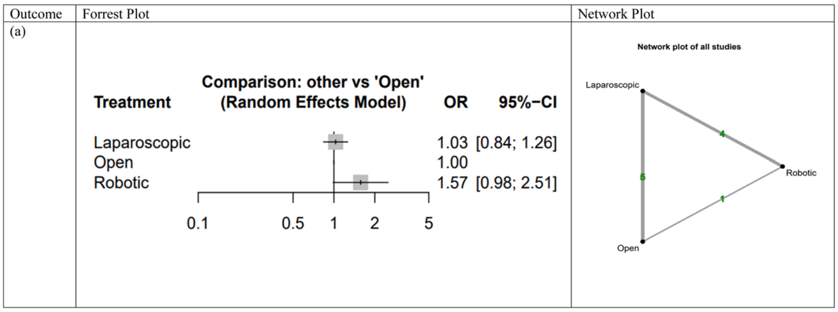

FIGURE 4 | Forrest and network plots with respect to oncological outcomes. (a) R0.

3.5.3 | IOBL

Overall, 92.3% of studies reported mean IOBL (12 studies). Overall, the mean IOBL was 333.1 mL. OLR had the highest mean IOBL (413.8 mL—10 studies), followed by LLR (283.9 mL—11 studies) and RLR (266.8 mL—four studies). At NMA, both LLR (MD −135.76, CI −240.35 to −31.17) and RLR (MD −204.85, CI −398.36 to −11.34) demonstrated a significant reduction in IOBL compared to OLR (Figure 4c).

3.5.4 | Conversion to Open

In total, 61.5% reported the requirement to convert to open (eight studies). Overall, 10.0% of patients required conversion to an open procedure (338/3380). More patients who underwent LLR (10.4%, 328/3166—eight studies) required conversion to open than those who underwent RLR (4.7%, 10/214—three studies). At NMA, patients who underwent LLR (OR 27.50, CI 7.73–97.48) were more likely to convert to open when compared to those who underwent RLR (Figure 4d).

3.5.5 | Blood Transfusion

Overall, 76.9% reported data on blood transfusion requirement (10 studies). In total, 16.9% of patients required blood transfusion (1051/6236). Patients who underwent LLR had the highest blood transfusion requirement (20.5%, 676/3303—10 studies), followed by OLR (358/2729—seven studies) and RLR (8.8%, 18/204—three studies). At NMA, there was a significant reduction in blood transfusion requirement favouring RLR (OR 0.13, 95% CI 0.05–0.32) while those undergoing LLR were as likely to require blood transfusions compared to OLR (OR 0.62, CI 0.38–1.02) (Figure 4e).

3.5.6 | Postoperative Complications

Overall, 76.9% of studies reported postoperative complications (10 studies). In total, 22.6% were reported to have postoperative complications (420/1861). OLR had the highest rates of postoperative complications (26.4%, 262/992—seven studies), followed by RLR (23.6%, 45/191—four studies) and LLR (16.6%, 113/678—eight studies). At NMA, both LLR (OR 0.50, CI 0.37 – 0.68) and RLR (OR 0.52, CI 0.32–0.86) significantly reduced postoperative complications relative to OLR (Figure 4f).

3.5.7 | LOS

In total, 53.8% of studies reported LOS (seven studies). Overall, the mean LOS was 8.6 days. OLR had the highest mean LOS (12.9 days—five studies), followed by LLR (6.7 days—six studies) and RLR (6.2 studies—four studies). When compared to OLR at NMA, patients undergoing LLR had a significantly reduced LOS (MD: −6.66, 95% CI: −11.6 to −1.88), with no difference observed with those undergoing RLR (MD: −5.06, 95% CI: −10.9 – 0.89) (Figure 4g).

4 | Discussion

There have been significant improvements in the surgical management of CRLM over recent decades, as evident from the data compiled in the current study [44]. Notwithstanding resection remaining the cornerstone of curative-intent treatment, multimodal therapeutic strategies have come into vogue in recent years, with cytotoxic chemotherapy and ablation techniques being adopted into practice to increase amenability for resection [45], which has directly translated into enhanced survival outcomes in certain incidences [46]. This study was performed to establish the surgical and oncological safety of newer MIS techniques compared to conventional OLR, and incorporated data from 6582 patients with CRLM across 13 studies of varying scientific quality. The results of this analysis demonstrate the noninferiority of LLR and RLR relative with OLR in the management of CRLM, with similar R0 resection rates, DFS and OS observed. Furthermore, MIS approaches were associated with improved surgical outcomes, including reduced IOBL, complication rates, and reduced LOS. These results are of clinical significance as robotic surgery comes into vogue for hepatopancreaticobillary resections, in particular when considering the recent robotic hepatopancreaticobillary surgery (ROBOT4HPB) Jury-Based Consensus which deemed robotic surgery acceptable for both minor and major liver resections [47].

The adoption of laparoscopic and RLRs have overtaken the traditional open resection in the contemporary management of CRLM [15, 48], with the results of the current study ratifying the this transition due to comparable oncological and survival outcomes being observed for both RLR and LLR. Importantly, this study demonstrated that the anticipated survival outcomes following LLR were to that of those undergoing OLR at 1-, 3-, and 5-year follow-up, respectively. These results were echoed in the analysis for DFS, with a nonsignificant difference observed at 1- and 3-year, respectively. While the lack of data available to facilitate analyses on 5-year outcomes for DFS may face scrutiny, it is important to note that the vast majority of those who succumb to recurrence in CRC typically recur in the 48 months following curative treatment, thus ratifying these results [49].

Importantly, there was no long-term survival or recurrence data for available for RLR which may bring into question the oncological safety of performing robotic resections in dealing with CRLM. Nevertheless, the adoption of robotic surgery into other subspecialties of surgical practice has indicated consistently that there is comparable long-term oncological outcomes anticipated following robotic- and laparoscopic-assisted procedures, which is apparent from data presented in a meta-analysis of five nonrandomised studies which included 986 patients and demonstrated similar 5-year OS (hazard ratio [HR] 0.77, 95% CI 0.57–1.04) and DFS (HR 1.04, 95% CI 0.77–1.40) for RLR relative with LLR [50]. However, these authors included studies performing resections of liver primary cancers as well as CRLM. While the early data (i.e., 1-year and 3-year OS and DFS) demonstrate similar outcomes for those undergoing robotic resection, it is likely that once the longer-term follow-up data ripens, these outcomes should replicate those of other malignancies with outcomes comparable to LLR and OLR for those undergoing RLR.

The data in this study supported MIS techniques in improving postoperative surgical outcomes in those undergoing resection for CRLM. Herein, both LLR and RLR reduced IOBL, postoperative complications and LOS, while patients who underwent LLR had a shorter anticipated LOS and those undergoing RLR were less likely to require blood transfusions during their perioperative course. Importantly, these findings ratify the data of the ROBOT4HPB consensus which suggested that robotic resections performed using the *Da Vinci* (Intuitive Surgery Incorporated, Sunnyvale, CA) shared similar postoperative outcomes with laparoscopic approach, while being less likely to be converted to open (note: all included studies included data from *Da Vinci* platforms X and Xi as recommended in the ROBOT4HPB consensus) [47]. Moreover, a previous review performed by Lo et al. suggested that lower IOBL, LOS, and lower rates of perioperative complications should be expected following MIS techniques when compared with OLR, with is replicated in the results of the current [51]. In addition, this study demonstrated similar intraoperative complications following MIS techniques, while also highlighting that patients who underwent LLR were more likely to convert to open relative to RLR, an interesting finding given the theoretical learning curve suggested surrounding novice use of robotic surgery. In this context, this study provides solid evidence supporting the comparability of LLR and RLR to traditional OLR, which secondary data (i.e., surgical and perioperative outcomes) from this study favour the use of MIS techniques for liver resection for CRLM. Given the theoretical advantages of MIS techniques, such as a reduced physiological stress and immunologic impact on patients, quicker postoperative recovery times, fewer anticipated complications, as well as decreased immediate and long-term strain on healthcare resources [52], MIS should be utilised where feasible.

This analysis is subject to several limitations. Firstly, only one of the 13 included studies was of prospective, RCT methodology, with 10 of included studies being of retrospective design, implying likely exposure to selection, confounding and ascertainment biases. Secondly, the reduced proportion of patients representing the RLR group limits the conclusions which may be drawn, which is relevant pertaining particularly to the long term (i.e., 5-year) DFS and OS data. Thirdly, various competing factors are likely to confound the results of this study, including the pragmatism of using of (neo)adjuvant chemotherapy, radiotherapy, or immunotherapy to enhance survival outcomes. Fourthly, based on the lack of available data, the authors were unable to perform an analysis of the cost effectiveness of each approach to CRLM. Finally, the impact of surgeon-specific proficiency, volume-outcome relationship (Birkmeyer effect) and the centralisation of CRLM treatment could not be formally assessed in this analysis [53].

In conclusion, this study demonstrates the oncological safety of LLR and RLR approaches for CRLM, with favourable surgical and perioperative outcomes anticipated following minimally invasive approaches. While these data are limited in the reliance upon studies of moderate methodological quality, these results are promising in supporting the ever-growing transition towards less aggressive surgical and therapeutic strategies. Nevertheless, the provision of well-designed RCTs will be required to fully ratify these results and quantify the true oncological and surgical safety of MIS approaches to CRLM.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data are available on request from the authors.

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