Review

Open Access

Check for updates

Minimally invasive approaches to intrahepatic cholangiocarcinoma

Alexandra M. Adams¹, Hop S. Tran Cao²

¹Department of Surgery, Brooke Army Medical Center, San Antonio, TX 78234, USA. ²Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA.

Correspondence to: Dr. Hop S. Tran Cao, Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX 77030, USA. E-mail: HSTran@mdanderson.org

How to cite this article: Adams AM, Tran Cao HS. Minimally invasive approaches to intrahepatic cholangiocarcinoma. *Mini-invasive Surg* 2023;7:18. https://dx.doi.org/10.20517/2574-1225.2023.12

Received: 15 Feb 2023 First Decision: 6 Apr 2023 Revised: 4 May 2023 Accepted: 18 May 2023 Published: 26 May 2023

Academic Editors: Zenichi Morise, Giulio Belli Copy Editor: Dong-Li Li Production Editor: Dong-Li Li

Abstract

While the incidence of intrahepatic cholangiocarcinoma (ICC) is increasing, few patients are surgical candidates, and recurrence rates remain high. Surgical resection remains the only potential curative therapy for ICC, and many retrospective cohorts have demonstrated comparable short-term and long-term outcomes between open, laparoscopic, and robotic liver resection (RLR) for ICC. However, rates of lymphadenectomy remain low amongst all groups, especially in laparoscopic approaches, despite its role in prognostication and therapeutic management. RLR may offer many of the short-term benefits of laparoscopic liver resection (LLR) and facilitate adequate lymphadenectomy while also increasing the ability to access posterosuperior segments and perform major hepatectomies.

Keywords: Intrahepatic cholangiocarcinoma, laparoscopic liver surgery, robotic liver surgery

INTRODUCTION

Intrahepatic cholangiocarcinoma (ICC) is the second most common primary liver malignancy after hepatocellular carcinoma (HCC), and its incidence is increasing worldwide^[1-3]. While the only curative therapy is surgical resection, only 15% of patients present with resectable disease^[4,5]. Even with surgical resection, median survival ranges from 27 to 36 months, and disease recurrence will occur in two-thirds of patients^[6]. In light of these statistics, systemic therapy is considered standard of care for all patients with



© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, sharing, adaptation, distribution and reproduction in any medium or format, for any purpose, even commercially, as

long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.





ICC, including those with resectable disease^[7]. Therefore, a surgical approach that supports rapid recovery and return to function with minimal disruption to quality of life is especially appealing.

Minimally invasive surgical (MIS) approaches, particularly laparoscopic liver resection (LLR), are well described in the treatment of HCC and colorectal liver metastasis and are associated with improved short-term outcomes^[8-11]. However, MIS treatment of ICC, whether via LLR or robotic liver resection (RLR), has not been well-studied, and its description is mostly limited to retrospective single-center studies from high-volume, expert centers. For instance, in a large systematic review including 2,804 patients comparing open liver resection (OLR) to LLR for malignant liver tumors, ICC was lumped with other metastatic liver tumors and altogether only accounted for 7% of included patients^[12]. With acknowledgment of the limited data, this review examines the state of the current literature comparing open, laparoscopic, and robotic approaches specific to ICC.

METHODS

This review aims to summarize the existing data on short-term and long-term outcomes of open, laparoscopic, and robotic approaches to surgical resection of ICC. PubMed was searched for terms including "intrahepatic cholangiocarcinoma," "minimally invasive," "laparoscopic", and "robotic", with a search end date of January 31, 2023. Short-term outcomes included operative time, percent conversion, intraoperative blood loss, major complications (Clavien Dindo grade 3a unless otherwise noted), length of stay, and 30-day mortality. Oncologic outcomes include percent of patients receiving Ro resection, lymph node dissection (LND), and ≥ 6 lymph nodes harvested. The long-term oncologic outcomes, including total percent recurrence, 1-year and 3-year overall survival (OS), and 1-year and 3-year disease-free survival (DFS), were also reported.

PRINCIPLES OF TREATMENT

Most patients are considered unresectable at presentation, as the tumor is often locally advanced or metastatic prior to causing symptoms^[4]. Contraindications to resection include metastatic disease, nodal disease beyond the regional basin (N2 disease), and invasion of the common hepatic artery or both the right and left hepatic arteries^[13-15]. Relative contraindications include multifocal tumors and portal vein involvement, although, in experienced centers, portal vein resections and reconstructions may be performed in selected patients^[16,17]. In addition, due to the tendency of ICC for intraductal and periductal spread, major hepatectomies are often required, necessitating a sufficient future liver remnant (FLR) or sufficient hypertrophy of the FLR following augmentation strategies such as portal vein embolization (PVE)^[18,19].

Few patients present with resectable disease, and surgery remains the only potentially curative treatment for ICC^[5,13,20]. Principles of surgical resection include total excision of the tumor with negative margins and removal of locoregional nodes, particularly stations 8 and 12^[6,15,21-23]. There is no evidence to support the need for an anatomic resection as long as negative margins can be obtained. Even at the time of surgery, resectable ICC is associated with lymph node metastases in 40% of patients, and LND should be performed routinely^[24]. The sth edition of the AJCC classification system recommends harvest of at least 6 nodes for adequate staging^[25].

While minimally invasive approaches are often associated with less morbidity, improved quality of life, and shorter length of stay, this approach cannot compromise the basic oncologic tenets of negative surgical margins and adequate LND. High-quality data are lacking regarding these critical aspects of MIS management of ICC, but many retrospective cohort studies have evaluated its feasibility, short-term outcomes, and oncologic outcomes. It is important to interpret these studies in the context of inherent

selection biases.

OPEN VERSUS LAPAROSCOPIC APPROACHES

Short-term outcomes

Many retrospective cohort studies have compared short-term outcomes of LLR *vs*. OLR. A meta-analysis by Regmi *et al.* compiled results from eight retrospective studies and compared short-term results of LLR *vs*. OLR for ICC. Length of stay was demonstrated to be notably shorter (P = 0.05), and overall morbidity rates were lower with LLR compared to OLR (P = 0.002). Duration of the operation and intraoperative blood loss were comparable between groups (P = 0.10), but the need for intraoperative blood transfusion was lower in the LLR group (P = 0.005). There was no difference in perioperative mortality between groups (P = 0.62)^[26].

A more recent retrospective cohort study supports these findings, comparing consecutive patients between 2011 to 2021 undergoing LLR *vs.* OLR for ICC. Short-term outcomes, including operation duration, surgical margins, and intra- and post-operative transfusion, did not differ significantly between the groups, but length of stay was shorter for the LLR group (8.8 *vs.* 10.6 days, P = 0.031). Major complications were higher in the OLR group, although not statistically different (3.3% *vs.* 12.3%, P > 0.05). Notably, however, there were differences in the size of the tumors and the extent of hepatectomy. The tumor diameter was larger in the OLR group (4.7 cm *vs.* 5.7 cm, P = 0.053). Larger resections were performed in the OLR group compared to the LLR group, including more trisectionectomy and hemihepatectomy (0.0% *vs.* 3.1%, 56.7% *vs.* 81.5%, P = 0.007)^[27]. This suggests that while short-term outcomes of LLR may be acceptable and even superior to OLR, these findings are at least partially reflective of a patient selection process to choose the appropriate LLR candidates.

This bias was again shown in a larger multicenter study from Europe by Sahakyan *et al.*, which compared LLR to OLR for ICC^[28]. Prior to matching, there was a significant difference in many baseline preoperative characteristics: OLR was associated with a higher rate of bilobar disease (6% *vs.* 25%, P < 0.01) and major liver resection (38% *vs.* 64.7%, P < 0.01). Cases were then matched for patient age, American Society of Anesthesiologists (ASA) grade, size, location and number of tumors, and underlying liver disease. After matching, rates of major complications and transfusions were similar between the two groups, but OLR was associated with longer length of stay (5 *vs.* 8 days, P < 0.01), longer operative durations (209 *vs.* 294 minutes, P < 0.01), more reoperations (4% *vs.* 16%, P = 0.046), and more overall complications (30% *vs.* 52%, P = 0.025)^[28].

Multiple other cohort studies have examined these short-term outcomes between LLR and OLR and demonstrated comparable operative durations, major complication rates, and mortality rates. The available data seem to consistently support shorter length of stay and less intraoperative blood loss when comparing LLR to OLR [Table 1]. Rates of Ro resection also remain comparable between approaches [Table 2].

Rates of lymphadenectomy

As previously mentioned, LND is recommended as standard of care in the surgical management of ICC at the very least for staging and prognostication purposes and to guide decision-making vis-à-vis adjuvant therapies^[24,25]. Current guidelines propose a minimum of 6 lymph nodes for adequate $LND^{[24]}$. Locoregional control and even survival may improve with the performance of $LND^{[24,29,30]}$, although the survival benefits remain debated^[31,32]. Adequate LND generally includes stations 8 and 12 [Figure 1], with one study demonstrating improved DFS and OS with inclusion of these stations, although this difference was not statistically significant (P = 0.080 and P = 0.078, respectively)^[33]. Even in lymph node-positive disease, surgical resection with LND may be associated with improved survival^[34,35]. Yet, there is a general failure to

First Author, Year, Design	Approach	n	Tumor Size, cm	Major Hep., %	Operative Time, min	Conversion, %	Intraoperative Blood Loss, ml (mean)	Major complications, %	Length of stay (days)	30-day Mortality, %
Uy, 2015 SI RC ^[52]	LLR OLR	11 26	4.15 4.25ª	54.5 84.6	272.5 335°	NR	325 750* ^a	9.1 26.9	9 11 ^ª	NR
Lee, 2016 <i>SI RC</i> ^[53]	LLR OLR	14 23	3.5 4.0 ^ª	50.0 82.6	255 330 [°]	NR	325 625* ^a	17.4 21.4	15 20 ^ª	NR
Wei, 2017 <i>SI RC</i> ^[54]	LLR OLR	12 20	5.25 6ª	58.3 55	212 230ª	16.7	350 350 [°]	16.7 15	14 11 ^a	0 0
Zhu, 2019 Sł _I RC, PSM [[]	LLR OLR	18 36	6 6	55.6 61.1	225 190*ª	11.1	200 300ª	5.6 11.1	6 6ª	0 0
Martin, 2019 Patabase ^{[40}	LLR OLR	312 1997	5.01 6.40* ^b	37.8 54.5*	NR	NR	NR	NR	NR	NR
Kinoshita, 2019 <i>MI RC</i> ^[56]	LLR OLR	15 21	2.6 3.4 ^b	NR	360 358 ^ª	NR	150 500°	13 19	NR	NR
Hobeika, 2020 MJ RC, PSM	LLR OLR	109 109	NR	47.7 47.7	240 263ª	13.8	200 346* ^a	22.9 26.6	7 14* ^a	5.5 3.7
Kang, 2020 ŞJ _J RC, PSM [[]	LLR OLR	24 24	4.7 4.1 ^b	75 75	407.2 316.4 ^b	20	1717.2 800.0 ^b	70.8 79.2 ^c	8.9 15.3* ^b	NR
Wu, 2020 SI RC ^[57]	LLR OLR	18 25	NR	33 52	305 300ª	NR	375 500* ^a	6 8	6 9* ^a	0 4
Haber, 2020 <i>SI RC</i> ^[58]	LLR OLR	27 31	6.0 6.5ª	70 78	314 282ª	7	NR	19 32	10 12* ^a	7 0
Ratti, 2021 SI_RC, PSM [[]	LLR OLR	150 150	5.3 5.8 ^b	34 36.7	270 230 ^b	11.3	150 350* ^b	4 8	4 6 ^a	1.3 1.3
Wang, 2022 SI RC ^[27]	LLR OLR	30 65	4.7 5.7⁵	56.7 81.5*	231 225.3 ^b	20	200 300* ^b	3.3 12.3	8.8 10.6* ^b	0 0
Sahakyan, 2022 MgRC, PSM	LLR OLR	50 50	5.5 5.8 ^b	38 74*	209 294* ^b	10	NR	24 38	5 8* ^a	4 10 ^d
Brustia, 2022 Database, PSM ^[59]	LLR OLR	89 89	4.67 5.32 ^b	53.9 68.5	NR	17.9	NR	8.9 17.9	NR	NR
Hamad, 2022 Patabase ^{[48}	RLR OLR	72 1804	5.1 6.8 ^b	45.5 67.3*	NR	8.3	NR	NR	5.8 8.9* ^b	2.2 3.0
Shapera, 2022 SI RC ^[60]	RLR OLR	15 19	5.5 4.5 ^b	87 95	331 356 ^b	NR	100 420* ^b	13 26.3	4 7 ^b	6.7 5.3

Table 1	. Short-Terr	n Outcomes of	Laparoscopic	c vs.Robotic vs.O	pen Liver Resection	for Intrahepatic	Cholangiocarcinoma
					F		

Outcome Definitions: Major hepatectomy: 3 consecutive liver segments^[61]. Major complications: Clavien-Dindo grade IIIa complications unless otherwise noted. Hep: Hepatectomy; SI: Single institution; RC: retrospective cohort; LLR: Laparoscopic liver resection; OLR: open liver resection; NR: not reported; PSM: propensity-score matched (matched data presented); MI: multi-institution; RLR: robotic liver resection. *Designates statistical significance. ^aReported as median. ^bReported as mean. ^cIncluded Clavien-Dindo grade II and above complications. ^dReported as 90-day mortality.

adhere to these recommendations at the broad national level, with a National Cancer Database (NCDB) study demonstrating a low overall rate of LND for 58.2% of ICC cases and only 24.8% with an adequate examination of 6+ lymph nodes per guidelines^[36]. In fact, if there is a major deficiency of LLR in the

First Author, Year, Design	Approach	n	RO Resection, %	Lymph Node Dissection, %	6 Lymph nodes, %
Uy, 2015 <i>SI RC</i> ^[52]	LLR OLR	11 26	NR	9.1 73.1	NR
Lee, 2016 <i>SI RC</i> ^[53]	llr Olr	14 23	NR	35.7 65.2	NR
Wei, 2017	llr	12	100	33.3	NR
SI RC ^[54]	Olr	20	95	55	
Zhu, 2019	llr	18	94.4	38.9	NR
<i>SI RC, PSM</i> ^[55]	Olr	36	94.4	41.7	
Martin, 2019	llr	312	81.3	48.5	8.7
Database ^[40]	Olr	1997	76.9*	61.2*	15.4*
Kinoshita, 2019	LLR	15	93.3	40	NR
<i>MI R</i> C ^[56]	OLR	21	95.2	33	
Hobeika, 2020	LLR	109	86.2	33.9	14.7
<i>MI RC, PSM</i> ^[38]	OLR	109	87.2	73.4*	25.7*
Kang, 2020 <i>SI RC, PSM</i> ^[37]	llr Olr	24 24	NR	25.0 75.8*	NR
Wu, 2020 SI RC ^[57]	llr Olr	18 25	(only RO resections included in the study)	NR	33 32
Haber, 2020	llr	27	89	85	NR
<i>SI RC</i> ^[58]	Olr	31	74	94	
Ratti, 2021	llr	150	97.3	88	NR
<i>SI RC, PSM</i> ^[42]	Olr	150	95.3	90	
Kim, 2022 Database ^[36]	LLR RLR OLR	3262 175 5174	88.4 90.1 85.1	45.9 43.6 61.1*	24.3 35.3 26.7
Wang, 2022SI RC ^[27]	llr	30	96.7	20.0	0
	Olr	65	95.4	56.9*	10.8*
Sahakyan, 2022	llr	50	84	20	NR
MI RC, PSM ^[28]	Olr	50	84	60*	
Brustia, 2022 <i>Database, PSM</i> ^[59]	llr Olr	89 89	84.0 70.0	NR	NR
Hamad, 2022	RLR	72	80.6	47.2	NR
Database ^[48]	OLR	1804	81.6	55.3	
Shapera, 2022 SI RC ^[60]	RLR OLR	15 19	86.7 63.2	NR	NR

 Table 2. RO Resection and Lymphadenectomy Rates in Laparoscopic vs.Robotic vs.Open Liver Resection for Intrahepatic

 Cholangiocarcinoma

SI: Single institutional; RC: retrospective cohort; LLR: Laparoscopic liver resection; OLR: open liver resection; NR: not reported; PSM: propensity score matched (matched data presented); MI: multi-institutional; RLR: robotic liver resection. *Designates statistical significance.

treatment of ICC in the existing literature, it is the lower rate of LND performed with this approach. This is generally attributed to technical difficulty of this procedure and likely remains one of the major barriers to and shortcoming of the adoption of LLR for ICC^[21,22].

Across the literature, rates of adequate LND are low overall, with large differences between OLR and LLR [Table 2]. Rates of LND were 30% in LLR *vs.* 75.4% in OLR (P < 0.001) in the retrospective cohort detailed by Kang *et al.*, a difference that persisted after propensity matching^[37]. Similar differences were observed in a French nationwide propensity-matched cohort by Hobeika *et al.*, with LND in 33.9% of LLR and 73.4% of OLR, and even yield of 6 lymph nodes in only 14.7% of LLR and 25.7% of OLR^[38]. Lee *et al.* also observed a similar difference in their series, with rates of 35.7% in LLR *vs.* 65.2% in OLR (P = 0.101), as did Wang *et al.* with 20.0% in LLR *vs.* 56.7% in OLR (P = 0.001)^[27,39]. Even in a national database study including 2,309 patients undergoing liver resection for ICC, significantly fewer LLR patients received any lymph node evaluation compared to OLR (39% *vs.* 61%, P < 0.001). Even more striking, the rate of an adequate LND of



Figure 1. Lymph node stations included in lymph node dissection for intrahepatic cholangiocarcinoma, particularly stations 12 (hepatoduodenal ligament) and station 8 (common hepatic artery). The depicted nodal stations include station 1 (right cardiac), station 3 (lesser gastric curvature), station 5 (supra-pyloric), station 7 (left gastric artery), station 8 (common hepatic artery), station 9 (celiac axis), station 12 (hepatoduodenal ligament), station 13 (posterior pancreatic), and station 16 (abdominal aortic)^[33].

6 lymph nodes was exceedingly low in both groups (9% vs. 15%, P < 0.001)^[40].

Historically, a need for extensive portal lymphadenectomy was considered a contraindication to LLR^[12]. However, a propensity-score-based, case-matched analysis by Ratti *et al.* demonstrates that laparoscopic LND for biliary malignancy is not only feasible but can result in adequate lymph node yield while also providing benefits of lower blood loss, fewer intra- and post-operative blood transfusions, and shorter length of stay compared to open LND. In addition, both overall and lymphadenectomy-related morbidity was similar between groups. Notably, this was a single-center study at a tertiary referral center at the Hepatobiliary Surgery Division of San Raffaele Hospital, Milano describing experiences after implementing institutional policy to mandate LND in both MIS and OLR^[41]. Their findings support that a minimally invasive approach to ICC is feasible and can still be oncologically sound in technically proficient hands.

Oncologic outcomes

Few studies have investigated differences in oncologic outcomes between LLR and OLR [Table 3]. Kang *et al.* compared 3-year OS and DFS within the cohort from 2004 to 2015 in their center with 1:1 propensity-score matching for age, gender, tumor location, extent of hepatectomy, and nodularity. There were no statistical differences between 3-year DFS or OS between the LLR and OLR groups before or after matching. Prior to matching, 3-year OS for patients undergoing LLR *vs.* OLR were 76.7% and 81.2% (P = 0.621), respectively, and 3-year DFS were 65.6% and 42.5% (P = 0.122). After matching, rates became more similar between LLR and OLR with 3-year OS of 74.8% and 75.5% (P = 0.710) and 3-year DFS of 59.9% and 41.8% (

First Author, Year, Design	Approach	n	Median Follow-Up, months	Total Recurrence, %	1-yr Overall Survival, %	3-yr Overall Survival, %	1-yr Disease- Free Survival, %	3-yr Disease- Free Survival, %
Uy, 2015 SI RC ^[52]	LLR OLR	11 26	17 overall	36.4 46.3	NR	77.9 66.2	NR	56.2 39.4
Lee, 2016 SI RC ^[53]	LLR OLR	14 23	15 35	21.4 43.4	NR	84.6 75.7	NR	76.9 56.7
Wei, 2017 SI RC ^[54]	llr Olr	12 20	17.5 12	50 60	NR	56.3 32.7	NR	43.8 27.9
Zhu, 2019 <i>SI RC, PSM</i> ^[55]	llr Olr	18 36	24 overall	55.6 61.1	66.7 72.2	45.8 38.2	53.1 48.7	37.8 34.9
Kinoshita, 2019 <i>MI RC^[56]</i>	LLR OLR	15 21	26 overall	NR	86 84	58 78	66 80	49 65
Kang, 2020 SI RC, PSM ^[37]	llr Olr	24 24	29 29.2	NR	NR	74.8 75.6	NR	59.9 41.8
Wu, 2020 SI RC ^[57]	llr Olr	18 25	NR	100.0 96.0	76.9 43.1	47.1 20.0	27.8 24.0	0.0 4.0
Ratti, 2021 <i>SI RC, PSM</i> ^[42]	llr Olr	150 150	NR	59.3 63.3	NR	NR	NR	NR
Sahakyan, 2022 <i>MI RC, PSM</i> ^[28]	LLR OLR	50 50	51 overall	25 22	NR	55.8 56	59.4 62.4	40 38.3
Brustia, 2022 Database, PSM [[]	LLR OLR	89 89	NR	NR	92 92	75 58 *	71 61	41 37
Wang, 2022 SI RC ^[27]	LLR OLR	30 65	13.8 10.7	33.3 44.6	75.7 71.3	52.0 51.1	63.4 71.3	41.7 53.5

Table 3. Long-Term Outcomes of Laparoscopic vs. Open Liver Resection for Intrahepatic Cholangiocarcinoma

SI: Single institutional; RC: retrospective cohort; LLR: Laparoscopic liver resection; OLR: open liver resection; NR: not reported; PSM: propensity score matched (matched data presented); MI: multi-institutional. *Designates statistical significance.

$P = 0.350)^{[37]}$.

Lee *et al.* also examined survival outcomes in their smaller cohort of 39 patients undergoing hepatectomy from 2010 to 2015 and found similar 3-year DFS and OS between groups. Comparing LLR and OLR, 3-year OS was 84.6% and 75.7% (P = 0.672), and 3-year DFS was 76.9% and 56.7 (P = 0.456), respectively. Even when comparing subgroups of patients who did or did not receive LND, as LND was significantly more common in the OLR group, there was no difference in OS or DFS between approaches^[39].

Another cohort at a large Italian tertiary center found LLR to be non-inferior in oncologic outcomes compared to OLR in terms of overall and DFS. Notably, the patients who underwent LLR had a shorter median time to adjuvant treatment than those who underwent OLR (35 *vs.* 49 days, P = 0.03), and a greater percentage received systemic adjuvant therapy at all (82.7% *vs.* 77.3%, P < 0.05)^[42].

While these studies are not randomized, multiple retrospective cohorts with and without propensity matching have demonstrated similar long-term oncologic outcomes in terms of recurrence and OS between LLR and OLR for ICC [Table 3].

ROBOTIC APPROACH

Robotic surgery has been growing in popularity, with benefits including increased dexterity, 3D visualization, surgeon comfort, and a quicker learning curve. Specific to minimally invasive liver resections, the robotic platform has increased the ability of the surgeon to perform major hepatectomies to safely access the posterosuperior segments and decrease conversions^[43-46]. Although many retrospective cohorts have also



Figure 2. Complete robotic portal lymphadenectomy for intrahepatic cholangiocarcinoma, with indocyanine green (Firefly) to highlight biliary anatomy.

demonstrated increased R0 resection rates between RLR and LLR for hepatic malignancies, this difference has not been borne out in a meta-analysis^[47].

Studies specific to the robotic approach for ICC are sparse but promising. An NCDB study only identified 72 robotic-assisted cases for stages I-III ICC between 2004 and 2017, compared to 1,804 open cases. Examining short- and long-term outcomes between RLR and OLR, they found no differences between the rate of R0 resection, post-operative morbidity, or long-term survival while reducing the length of hospital stay (6 *vs.* 9 days, P = 0.019). Notably, there was no difference in LND between groups, which is a striking contrast to studies comparing LLR to OLR^[48].

The robotic approach was also demonstrated to improve LND rates and retrieval of at least 6 nodes in another NCDB analysis by Kim *et al.*, which examined open *vs.* laparoscopic *vs.* robotic approaches for both ICC and gallbladder cancer (GBC). In fact, rates of both R0 resection and retrieval of 6+ nodes were highest within the RLR group in the combined ICC and GBC group. For ICC only, comparing LLR *vs.* RLR *vs.* OLR, R0 resection was achieved 88.4% *vs.* 90.1% *vs.* 85.1%, respectively (P = 0.061), and retrieval of 6+ nodes in 24.3% *vs.* 35.3% *vs.* 26.7% (P = 0.338), respectively. Rates of LND were highest in the OLR group yet low regardless of approach, 45.9% *vs.* 43.6% *vs.* 61.1% (P < 0.001), respectively. Performance of surgery at high volume and academic centers predicted R0 resection and adequate lymphadenectomy regardless of approach^[36].

One of the largest benefits of RLR for biliary tract cancer may be improved lymphadenectomy rates while also preserving the other benefits of LLR, such as decreased length of stay, decreased morbidity with quicker recovery, and preserved long-term outcomes^[36,43]. Adjuncts, such as indocyanine green (ICG), can also be easier to utilize on the robotic platform and may help detect tumors and their margins, satellite lesions, or even metastases [Figure 2]^[49-51].

PATIENT SELECTION

Ultimately, any approach to surgical resection for ICC should include the basic principles of negative margins and adequate lymph node staging. Surgeons must account for their own technical proficiency and experience when selecting patients for a minimally invasive approach. Even at expert, high-volume centers,

specific tumor characteristics disqualified patients from a laparoscopic approach. These characteristics include lesions that require biliary or vascular resections, lesions infiltrating the inferior vena cava, and lesions in contact with the hepatic vein of the FLR^[42]. However, the robotic platform may expand the patient selection criteria due to more dexterity and technical capabilities, with increased ability to suture, dissect larger tumors, and access the posterosuperior segments^[45].

At our institution, we routinely offer MIS hepatectomy for ICC, and our preferred approach for this is the robotic platform, which, in our experience, has allowed for expanding criteria for MIS, reduced the learning curve, and facilitated the performance of LND, which should be standard practice for this disease. Of course, the experience and technical ability of the surgeon should also be taken into account, as individual surgeons should recognize the limit of their abilities on the MIS platform - as they should with open surgery - in deciding which patients should be offered this option. Guiding principles of Ro resection and adequate lymphadenectomy are crucial and cannot be discarded for the sake of a MIS approach. Academic centers and high-volume minimally invasive centers demonstrate the highest rate of achieving these oncologic principles and are associated with the best long-term outcomes for this highly select group of patients^[36].

CONCLUSION

Although high-quality, randomized data do not yet exist comparing open, laparoscopic, and robotic approaches to resection of ICC, multiple cohorts and meta-analyses demonstrate comparable short- and long-term outcomes between OLR and LLR. It should be noted that while we attempted to comprehensively include all studies specifically comparing surgical approaches for ICC, this is not a true systematic review nor meta-analysis, and conclusions must be drawn with caution, especially as it does not include any randomized data. Rather, we submit this review in the context of the approach of our group to the surgical treatment of ICC. Acknowledging the limitations of the data, benefits of LLR may include decreased length of stay and decreased morbidity while preserving survival outcomes. However, a major shortcoming in LLR is the decreased rate of LND, likely secondary to technical difficulty. The robotic platform may facilitate adequate lymph node harvest and expand minimally invasive options for more complex tumor locations and major hepatectomies.

DECLARATIONS

Authors' contributions

Made substantial contributions to the conception, outline, drafting, and editing of the manuscript: Adams AM, Tran Cao HS

Availability of data and materials Not applicable.

Financial support and sponsorship None.

Conflicts of interest All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate Not applicable.

Consent for publication

None.

Copyright

© The Author(s) 2023.

REFERENCES

- 1. Khan SA, Tavolari S, Brandi G. Cholangiocarcinoma: Epidemiology and risk factors. Liver Int 2019;39 Suppl 1:19-31. DOI PubMed
- 2. Shaib Y, El-Serag HB. The epidemiology of cholangiocarcinoma. *Semin Liver Dis* 2004;24:115-25. DOI PubMed
- 3. Shaib YH, Davila JA, McGlynn K, El-Serag HB. Rising incidence of intrahepatic cholangiocarcinoma in the United States: a true increase? *J Hepatol* 2004;40:472-7. DOI PubMed
- 4. Buettner S, van Vugt JL, IJzermans JN, Groot Koerkamp B. Intrahepatic cholangiocarcinoma: current perspectives. *Onco Targets Ther* 2017;10:1131-42. DOI PubMed PMC
- Spolverato G, Vitale A, Cucchetti A, et al. Can hepatic resection provide a long-term cure for patients with intrahepatic cholangiocarcinoma? *Cancer* 2015;121:3998-4006. DOI
- 6. Bridgewater J, Galle PR, Khan SA, et al. Guidelines for the diagnosis and management of intrahepatic cholangiocarcinoma. *J Hepatol* 2014;60:1268-89. DOI
- Primrose JN, Fox RP, Palmer DH, et al; BILCAP study group. Capecitabine compared with observation in resected biliary tract cancer (BILCAP): a randomised, controlled, multicentre, phase 3 study. *Lancet Oncol* 2019;20:663-73. DOI PubMed
- 8. Morise Z, Aldrighetti L, Belli G, et al; ILLS-Tokyo Collaborator group. Laparoscopic repeat liver resection for hepatocellular carcinoma: a multicentre propensity score-based study. *Br J Surg* 2020;107:889-95. DOI PubMed
- Morise Z, Ciria R, Cherqui D, Chen KH, Belli G, Wakabayashi G. Can we expand the indications for laparoscopic liver resection? A systematic review and meta-analysis of laparoscopic liver resection for patients with hepatocellular carcinoma and chronic liver disease. J Hepatobiliary Pancreat Sci 2015;22:342-52. DOI PubMed
- Fretland ÅA, Dagenborg VJ, Waaler Bjørnelv GM, et al. Quality of life from a randomized trial of laparoscopic or open liver resection for colorectal liver metastases. Br J Surg 2019;106:1372-80. DOI PubMed
- 11. Fretland ÅA, Kazaryan AM, Edwin B. Laparoscopic resection for liver malignancies: do the elderly benefit more? *J Invest Surg* 2019;32:83-4. DOI
- Nguyen KT, Gamblin TC, Geller DA. World review of laparoscopic liver resection-2,804 patients. Ann Surg 2009;250:831-41. DOI PubMed
- 13. Endo I, Gonen M, Yopp AC, et al. Intrahepatic cholangiocarcinoma: rising frequency, improved survival, and determinants of outcome after resection. *Ann Surg* 2008;248:84-96. DOI
- 14. Hyder O, Hatzaras I, Sotiropoulos GC, et al. Recurrence after operative management of intrahepatic cholangiocarcinoma. *Surgery* 2013;153:811-8. DOI PubMed PMC
- Ribero D, Pinna AD, Guglielmi A, et al; Italian Intrahepatic Cholangiocarcinoma Study Group. Surgical approach for long-term survival of patients with intrahepatic cholangiocarcinoma: a multi-institutional analysis of 434 patients. *Arch Surg* 2012;147:1107-13. DOI
- Spolverato G, Kim Y, Alexandrescu S, et al. Is hepatic resection for large or multifocal intrahepatic cholangiocarcinoma justified? Results from a multi-institutional collaboration. *Ann Surg Oncol* 2015;22:2218-25. DOI PubMed PMC
- 17. Abbas S, Sandroussi C. Systematic review and meta-analysis of the role of vascular resection in the treatment of hilar cholangiocarcinoma. *HPB* 2013;15:492-503. DOI PubMed PMC
- DeOliveira ML, Cunningham SC, Cameron JL, et al. Cholangiocarcinoma: thirty-one-year experience with 564 patients at a single institution. *Ann Surg* 2007;245:755-62. DOI PubMed PMC
- 19. van Lienden KP, van den Esschert JW, de Graaf W, et al. Portal vein embolization before liver resection: a systematic review. *Cardiovasc Intervent Radiol* 2013;36:25-34. DOI PubMed PMC
- Nakeeb A, Tran KQ, Black MJ, et al. Improved survival in resected biliary malignancies. Surgery 2002;132:555-63; discission 563. DOI
- 21. Weber SM, Ribero D, O'Reilly EM, Kokudo N, Miyazaki M, Pawlik TM. Intrahepatic cholangiocarcinoma: expert consensus statement. *HPB* 2015;17:669-80. DOI PubMed PMC
- 22. Maithel SK, Gamblin TC, Kamel I, Corona-Villalobos CP, Thomas M, Pawlik TM. Multidisciplinary approaches to intrahepatic cholangiocarcinoma. *Cancer* 2013;119:3929-42. DOI PubMed
- Muratore A, Ribero D, Zimmitti G, Mellano A, Langella S, Capussotti L. Resection margin and recurrence-free survival after liver resection of colorectal metastases. *Ann Surg Oncol* 2010;17:1324-9. DOI PubMed
- 24. Bagante F, Spolverato G, Weiss M, et al. Assessment of the lymph node status in patients undergoing liver resection for intrahepatic cholangiocarcinoma: the new eighth edition AJCC staging system. *J Gastrointest Surg* 2018;22:52-9. DOI
- 25. Spolverato G, Bagante F, Weiss M, et al. Comparative performances of the 7th and the 8th editions of the American Joint Committee on Cancer staging systems for intrahepatic cholangiocarcinoma. *J Surg Oncol* 2017;115:696-703. DOI
- 26. Regmi P, Hu HJ, Paudyal P, et al. Is laparoscopic liver resection safe for intrahepatic cholangiocarcinoma? A meta-analysis. *Eur J Surg Oncol* 2021;47:979-89. DOI

- 27. Wang J, Ma D, Du G, et al. Laparoscopic vs. open anatomical hepatectomy for intrahepatic cholangiocarcinoma: a retrospective cohort study. *Front Surg* 2022;9:1003948. DOI PubMed PMC
- Sahakyan MA, Aghayan DL, Edwin B, et al. Laparoscopic versus open liver resection for intrahepatic cholangiocarcinoma: a multicenter propensity score-matched study. *Scand J Gastroenterol* 2023;58:489-96. DOI
- 29. Vitale A, Moustafa M, Spolverato G, Gani F, Cillo U, Pawlik TM. Defining the possible therapeutic benefit of lymphadenectomy among patients undergoing hepatic resection for intrahepatic cholangiocarcinoma. *J Surg Oncol* 2016;113:685-91. DOI PubMed
- **30.** Yoh T, Cauchy F, Le Roy B, et al. Prognostic value of lymphadenectomy for long-term outcomes in node-negative intrahepatic cholangiocarcinoma: A multicenter study. *Surgery* 2019;166:975-82. DOI
- 31. Li F, Jiang Y, Jiang L, et al. Effect of lymph node resection on prognosis of resectable intrahepatic cholangiocarcinoma: a systematic review and meta-analysis. *Front Oncol* 2022;12:957792. DOI PubMed PMC
- 32. Sposito C, Droz Dit Busset M, Virdis M, et al. The role of lymphadenectomy in the surgical treatment of intrahepatic cholangiocarcinoma: a review. *Eur J Surg Oncol* 2022;48:150-9. DOI
- 33. Kim SH, Han DH, Choi GH, Choi JS, Kim KS. Extent of Lymph Node Dissection for Accurate Staging in Intrahepatic Cholangiocarcinoma. J Gastrointest Surg 2022;26:70-6. DOI PubMed
- 34. Guglielmi A, Ruzzenente A, Campagnaro T, et al. Patterns and prognostic significance of lymph node dissection for surgical treatment of perihilar and intrahepatic cholangiocarcinoma. *J Gastrointest Surg* 2013;17:1917-28. DOI
- Cao HS, Zhang Q, Sada YH, Chai C, Curley SA, Massarweh NN. The role of surgery and adjuvant therapy in lymph node-positive cancers of the gallbladder and intrahepatic bile ducts. *Cancer* 2018;124:74-83. DOI PubMed
- 36. Kim BJ, Newhook TE, Tzeng CD, et al. Lymphadenectomy and margin-negative resection for biliary tract cancer surgery in the United States-Differential technical performance by approach. *J Surg Oncol* 2022;126:658-66. DOI PubMed
- 37. Kang SH, Choi Y, Lee W, et al. Laparoscopic liver resection versus open liver resection for intrahepatic cholangiocarcinoma: 3-year outcomes of a cohort study with propensity score matching. *Surg Oncol* 2020;33:63-9. DOI
- Hobeika C, Cauchy F, Fuks D, et al; AFC-LLR-2018 study group. Laparoscopic versus open resection of intrahepatic cholangiocarcinoma: nationwide analysis. *Br J Surg* 2021;108:419-26. DOI PubMed
- **39.** Lee SJ, Kang SH, Choi Y, et al. Long-term outcomes of laparoscopic versus open liver resection for intrahepatic combined hepatocellular-cholangiocarcinoma with propensity score matching. *Ann Gastroenterol Surg* 2022;6:562-8. DOI PubMed PMC
- 40. Martin SP, Drake J, Wach MM, et al. Laparoscopic approach to intrahepatic cholangiocarcinoma is associated with an exacerbation of inadequate nodal staging. *Ann Surg Oncol* 2019;26:1851-7. DOI PubMed PMC
- Ratti F, Cipriani F, Ariotti R, et al. Safety and feasibility of laparoscopic liver resection with associated lymphadenectomy for intrahepatic cholangiocarcinoma: a propensity score-based case-matched analysis from a single institution. *Surg Endosc* 2016;30:1999-2010. DOI
- 42. Ratti F, Casadei-Gardini A, Cipriani F, et al. Laparoscopic Surgery for Intrahepatic Cholangiocarcinoma: A Focus on Oncological Outcomes. *J Clin Med* 2021;10:2828. DOI PubMed PMC
- 43. Kone LB, Bystrom PV, Maker AV. Robotic surgery for biliary tract cancer. Cancers 2022;14:1046. DOI PubMed PMC
- 44. Mejia A, Cheng SS, Vivian E, Shah J, Oduor H, Archarya P. Minimally invasive liver resection in the era of robotics: analysis of 214 cases. *Surg Endosc* 2020;34:339-48. DOI PubMed
- 45. Bozkurt E, Sijberden JP, Hilal MA. What is the current role and what are the prospects of the robotic approach in liver surgery? *Cancers* 2022;14:4268. DOI PubMed PMC
- Kamarajah SK, Bundred J, Manas D, Jiao L, Hilal MA, White SA. Robotic versus conventional laparoscopic liver resections: A systematic review and meta-analysis. Scand J Surg 2021;110:290-300. DOI PubMed
- Rahimli M, Perrakis A, Andric M, et al. Does robotic liver surgery enhance R0 results in liver malignancies during minimally invasive liver surgery?-A systematic review and meta-analysis. *Cancers* 2022;14:3360. DOI PubMed PMC
- 48. Hamad A, Ansari A, Li Y, et al. Short- and long-term outcomes following robotic and open resection for intrahepatic cholangiocarcinoma: a national cohort study. *Surg Oncol* 2022;43:101790. DOI
- Piccolo G, Barabino M, Lecchi F, et al. Laparoscopic indocyanine green fluorescence imaging for intrahepatic cholangiocarcinoma. *Am Surg* 2022:31348221103659. DOI
- 50. Franz M, Arend J, Wolff S, et al. Tumor visualization and fluorescence angiography with indocyanine green (ICG) in laparoscopic and robotic hepatobiliary surgery valuation of early adopters from Germany. *Innov Surg Sci* 2021;6:59-66. DOI PubMed PMC
- 51. Marino MV, Podda M, Fernandez CC, Ruiz MG, Fleitas MG. The application of indocyanine green-fluorescence imaging during robotic-assisted liver resection for malignant tumors: a single-arm feasibility cohort study. *HPB* 2020;22:422-31. DOI PubMed
- 52. Uy BJ, Han HS, Yoon YS, Cho JY. Laparoscopic liver resection for intrahepatic cholangiocarcinoma. *J Laparoendosc Adv Surg Tech* A 2015;25:272-7. DOI PubMed
- 53. Lee W, Park JH, Kim JY, et al. Comparison of perioperative and oncologic outcomes between open and laparoscopic liver resection for intrahepatic cholangiocarcinoma. *Surg Endosc* 2016;30:4835-40. DOI
- Wei F, Lu C, Cai L, Yu H, Liang X, Cai X. Can laparoscopic liver resection provide a favorable option for patients with large or multiple intrahepatic cholangiocarcinomas? *Surg Endosc* 2017;31:3646-55. DOI PubMed
- Zhu Y, Song J, Xu X, Tan Y, Yang J. Safety and feasibility of laparoscopic liver resection for patients with large or multiple intrahepatic cholangiocarcinomas: A propensity score based case-matched analysis from a single institute. *Medicine* 2019;98:e18307.

DOI PubMed PMC

- 56. Kinoshita M, Kanazawa A, Takemura S, et al. Indications for laparoscopic liver resection of mass-forming intrahepatic cholangiocarcinoma. *Asian J Endosc Surg* 2020;13:46-58. DOI PubMed
- 57. Wu J, Han J, Zhang Y, et al. Safety and feasibility of laparoscopic versus open liver resection with associated lymphadenectomy for intrahepatic cholangiocarcinoma. *Biosci Trends* 2020;14:376-83. DOI
- 58. Haber PK, Wabitsch S, Kästner A, et al. Laparoscopic liver resection for intrahepatic cholangiocarcinoma: a single-center experience. *J Laparoendosc Adv Surg Tech A* 2020;30:1354-9. DOI
- Brustia R, Laurent A, Goumard C, et al; AFC-ICC-2009; AFC-LLR-2018; PRS-2019 Study group. Laparoscopic versus open liver resection for intrahepatic cholangiocarcinoma: report of an international multicenter cohort study with propensity score matching. Surgery 2022;171:1290-302. DOI PubMed
- Shapera EA, Ross S, Syblis C, Crespo K, Rosemurgy A, Sucandy I. Analysis of oncological outcomes after robotic liver resection for intrahepatic cholangiocarcinoma. *Am Surg* 2022:31348221093933. DOI PubMed
- 61. Strasberg SM. Nomenclature of hepatic anatomy and resections: a review of the Brisbane 2000 system. *J Hepatobiliary Pancreat Surg* 2005;12:351-5. DOI PubMed