Review

Robotic liver surgery: literature review and current evidence

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Abstract

In the field of minimally invasive surgery, robotic surgery (RS) was introduced to overcome drawbacks in laparoscopic surgery. However, its clinical application in hepatobiliary surgery is not yet standardized. This review analyzed the results of RS to clarify the benefits of robotic liver surgery in comparison with standard laparoscopy. Among 112 publications found in the literature, the 72 most relevant were selected and the following data were extracted: patients characteristics, operative procedures, histopathology, short-term and long-term outcomes, and costs. Twenty-nine articles on robotic liver resections, published in the last five years (2015-2020) and including 1831 patients, were analyzed. Twenty-five comparative studies between robotic and laparoscopic surgery were evaluated to underline the differences in operative outcomes. Eventually, 4 sub-group analyses were conducted on hepatocellular carcinoma, gallbladder cancer, hilar cholangiocarcinoma, and colorectal liver metastases. Almost all the authors reported data on safety, feasibility and oncologic effectiveness of RS reaching comparable results with laparoscopy. However, even if robotic surgery showed longer operative time and higher costs, in selected cases it allowed to increase the rate of minimally invasive approach when compared with laparoscopy. Thus, both open and minimally invasive surgery should be provided in a modern hepatobiliary center, including the robotic approach particularly to complex cases, otherwise very demanding by laparoscopy. In conclusion, different techniques should be tailored to each patient, choosing the minimally invasive approach when possible, enhancing patients' recovery after surgery, especially in cirrhotic livers and in the context of liver transplantation. Although many centers experienced robotic liver surgery, more and larger studies are necessary to define its real benefits relative to laparoscopy, in order to standardize patient selection criteria and techniques.

INTRODUCTION

Since its introduction, robotic surgery (RS) has received great interest from scientific societies. In the era of minimally invasive surgery (MIS) it represents an advanced technique able to overcome some limitations of laparoscopy. Nevertheless, its use is not standardized in hepatobiliary surgery. Although single surgeons and centers have published their experiences demonstrating the safety and feasibility of the technique, large international studies are limited and few publications reported long-term outcomes. The advantages of RS are several: it provides increased surgical dexterity and enhanced suturing ability, thanks to a magnified three-dimensional view of the operative field, hand tremor filtration and articulating instruments with seven-degrees of freedom. Furthermore, this approach reduces significantly surgeons' fatigue, improving performances for long operations[1,2]. In addition, RS supports and upgrades the technology of specific surgical tools, that can help surgeons to face challenging situations and improve surgical results, such as with intraoperative ultrasound, near-infrared fluorescence with indocyanine green, CT and MR images integrated into the robotic console. The images can be simultaneously displayed with the operative field during liver parenchymal transection, allowing the surgeon to change the previously marked transection line if necessary and to detect further lesions, gaining adequate margins for malignancies[3-5]. On the contrary, current RS systems' disadvantages include the absence of a dedicated instrument for transection (i.e., CUSA), the need for additional surgeons and time for instrument replacement, the learning curve of the team to dock the instruments and the lack of haptic feedback[2]. Nonetheless, the development of skills and experience of the surgical team can significantly decrease the length of RS associated to the docking time and the replacement of the instruments[6]. Finally, one of the major drawbacks of RS are costs, limiting its use to selected surgical procedures and few centers. As a minimally invasive approach, RS allows improvement of almost all the parameters of postoperative recovery, such as pain control, oral intake, post-operative morbidity and length of hospital stay[7]. Recently, the Southampton international guidelines, providing indications and limits of liver MIS, advocated RS as a promising, but not yet standardized, approach[8]. The aim of this review was to analyze the results of robotic hepatobiliary surgery and to compare them with laparoscopy, in order to clarify the benefits and contraindications of RS.

METHODS

A search of the current literature on robotic liver surgery was conducted in PubMed, Medline, PMC and Google Scholar databases. The research terms adopted were: robotic/robot-assisted liver surgery/resection, hepatic robotic surgery/resection, robotic/robot-assisted hepatectomies. Only articles published in English were selected. Further reports were retrieved from those listed in the articles' references and from the manual search on specific additional topics, such as robotic surgery for hepatocellular carcinoma, cholangiocarcinoma, gallbladder cancer, colorectal liver metastases, lesions located in postero-superior liver segments, comparison between laparoscopic and robotic hepatic resections.

Among the 112 publications analyzed, the most significant were selected according to the following factors: quality of data reported and of statistical analysis adopted, relevance in scientific literature, date of publication. In case of overlapping studies with the same first author, the most recent was chosen. Once reviews, meta-analyses and studies reporting incomplete or unclear information were excluded, the following data were extracted from the 72 remaining publications: patient characteristics (number of patients, age, sex, body mass index, ASA score, comorbidities, previous chemotherapy and abdominal surgery), operative procedure (type of resection, use of Pringle maneuver, additional simultaneous procedures, intraoperative drain placement, estimated blood loss, operation time,
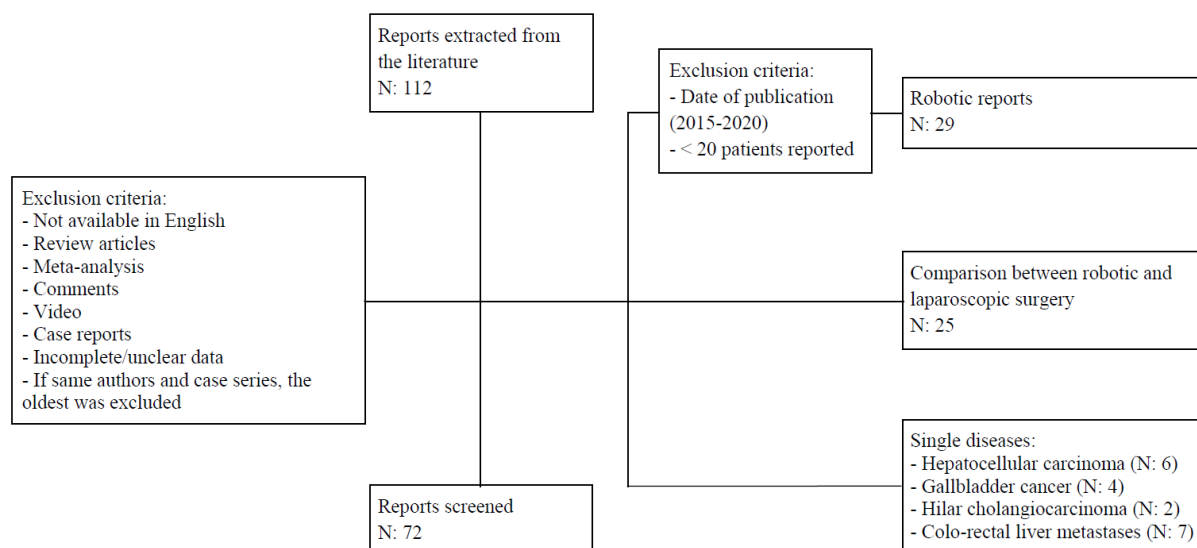
Figure 1. Selection of articles

conversion rate), histopathology (nature of the lesion, median tumor size, number of lesions, margin status, lymphadenectomy), short-term outcomes (overall morbidity, major complications, perioperative blood transfusions, admission to intensive care units, length of hospital stay, surgery-related readmission, reoperation within 30 days, 30- and 90-days mortality), long-term outcomes (disease free survival, overall survival), costs [Figure 1].

Minor and major resections were defined according to the Brisbane 2000 Terminology of Liver Anatomy and Resections[9]. The Clavien-Dindo Classification of surgical complications was adopted to define major complications as grade three or more[10]. Firstly, 29 publications on robotic liver surgery were selected and reviewed, excluding those reporting less than 20 patients. Secondly, 25 articles comparing robotic and laparoscopic liver resections were reviewed. Eventually, 4 sub-group analyses were conducted including studies on single malignant hepatobiliary diseases: hepatocellular carcinoma (HCC), gallbladder cancer (GBC), hilar cholangiocarcinoma (hCCC), colorectal liver metastases (CRLM).

RESULTS

Robotic liver surgery

Twenty-nine articles, published in the last five years (2015-2020) including a number of patients greater than or equal to 20, were analyzed [Table 1]. The total number of patients reported in 29 studies was 1831, with a median number of 61 patients (range 20-183). The median age was 61 years old (range 45-69.4). All the studies were retrospective and most of them reported cumulative results, without any differentiation between benign and malignant diseases or minor and major liver resections.

Type of liver resection
Referring to the type of resections, 1328 (69.5%) were minor, and 584 (30.5%) were major resections. The number of "technically major resections"[8] (segments 1, 4a, 7, 8) collected was 214 (11.7%). The studies including resections of these segments reported a longer operative time and greater estimated blood loss (EBL). Nota *et al.*[11] published a multi-institutional propensity score study (31 matchings), demonstrating that minor robotic resections of postero-superior segments were safe and feasible, improving outcomes in comparison with open surgery [median EBL 180 mL *vs.* 300 mL, operative time 198 min *vs.* 255 min, length of stay (LOS) 4 days *vs.* 10 days].

Table 1. Robotic liver surgery

Authors	Cases	Age	Location	Major/minor	EBL	Time	Conversion	Malignant	R0	LoS	Overall/Major complications
Chong et al.[1]	91	58.7	LS, Sg1	19/72	274.6*	259.3*	7.7	100	98.9	4.8	9.9/3.3
Montalti et al.[2]	36	62	PS	0/36	415*	306*	13.9	69.4	89	6*	19.4/11.1
Marino et al.[4]	40	69.4	LS	18/22	260	305	2.5	100	100	7.4	20/12.5
Pesi et al.[5]	51	63	LS, PS	13/38	100	300	2	100	100	5	18/9.8
Magistri et al.[6]	22	60.8	LS	2/20	400	318*	0	100	95.5	5.1	68.2/9
Nota et al.[11]	51	59	PS	0/51	180	198	8	88.2	84	4	-/6
Daskalaki et al.[12]	67	52.5	LS	29/39	438*	293.4*	8.8	55.8	-	6.8*	22/4.4
Hu et al.[13]	58	52.2	LS	0/58	80.1*	107*	0	62	100	4.3	1.7/-
Lee et al.[14]	70	58	LS	14/56	100	251.5	5.7	74.2	98.2	5	11.4/-
Felli et al.[15]	20	64.6	LS, PS	2/18	50	141.5*	0	85	-	-	-
Lai et al.[16]	95	62.1	LS, PS	27/75	334.6*	207.4	4	100	96	7.3*	14/1
Li et al.[17]	48	62.4	LS, Sg1	48/0	150	276	-	100	72.9	9	58.3/10.4
Guerra et al.[18]	59	64	LS, PS	4/78	200	210	12	100	92	6.7	27/5
Goel et al.[19]	27	54	LS	0/27	200	295	14.8	100	100	4	3.7/3.7
Khan et al.[20]	61	66	LS	8/53	100	240	11.5	100	85.2	5	37.7/11.4
Efanov et al.[21]	40	45	PS	2/49	465*	407	0	28	-	11	20/-
Choi et al.[22]	69	53	LS	64/16	170	491	9.1	76.8	100	8	43.5/10.6
Sham et al.[23]	71	54.8	LS, Sg1	17/54	495*	284*	5.7	98.6	-	3.9*	14.3/4.3
Fruscione et al.[24]	57	58.1	LS	57/0	250	194	-	64.9	91.9	4	28.1/25.1
Lim et al.[25]	61	66	LS, PS	9/52	-	277	0	100	89	9	25/2
Beard et al.[26]	115	61	LS, PS	17/98	-	272*	5.2	93.9	73.7	5	31.3/10.4
Quijano et al.[27]	21	59.3	LS, PS	4/17	-	262*	4.75	65	-	12*	19/4.7
Chen et al.[28]	183	60.8	LS, PS	92/91	249	361	1.6	67.2	-	7.5	4.4/2.1
Kingham et al.[29]	64	64	LS	6/65	100	163	6.3	78.2	-	-	10.9/4.4
Sucandy et al.[30]	75	64	LS	25/50	125	227	0	81	-	3	11/-
Wang et al.[31]	92	54.1	LS	92/0	243*	195.5*	1	66.3	-	7.4*	13/1.1
Melstrom et al.[32]	97	62	LS, PS	13/84	144*	197*	9.7	85.5	-	-	9.7/-
Ceccarelli et al.[33]	70	67	LS, PS	2/89	25	115*	10	70	94.3	3	10.1/1.4
Guadagni et al.[34]	20	66	LS	0/20	250*	198.5*	0	20	100	4.7	25/0

Cases: number of patients. Lesions' location: PS: postero-superior segments; LS: laparoscopic segments different from the postero-superiors; LLS: left-lateral sectionectomy. Major/minor resections: number of major/minor, according to the description of the authors or calculated from the data supplied. EBL: milliliters (median/*mean). Operative time: minutes (median/*mean). Conversion rate: percentage of procedures converted to open surgery. Malignant: percentage of malignant lesions. R0: percentage of negative margin status. LoS: days (median/*mean). Overall/major complications: percentage of all complications/major complications. "-": not reported

Surgery related factors

Among the 29 studies collected, the median value of EBL was 200 mL (range 25-495) and the median operative time was 260.65 min (range 107-491). Chong et al.[1] reported results of resections differentiated by difficulty scoring system (DSS). The authors confirmed a correlation between DSS and EBL and operative time. The mean EBL was 274.6 mL (146.4 mL for low difficulty resections and 646.7 mL for high difficulty resections), while the mean operative time was 259.3 min (205.9 min for low difficulty resections and 433.1 min for high difficulty resections)[35]. Daskalaki et al.[12] indicated the specific results of major and minor resections, showing higher EBL and conversion rate, longer operative time and LOS for major resections: mean EBL 354.7 mL *vs.* 570 mL, mean operative time 223.2 min *vs.* 404 min, conversion rate 2.5% *vs.* 17.2%, mean LOS 5.2 days *vs.* 8.8 days.

Only 10 articles reported data about the use of the Pringle maneuver and the median rate of its application was 23.6% (range 0-55.6). The agreement in the literature on this topic is limited and some authors considered pedicle clamping unnecessary in most cases during RS[13-15,36]. Otherwise, other authors preferred a routine use of pedicle clamping during major hepatectomies or for difficult resections[2,16-18].

Conversion to open surgery occurred with a median of 5.45% (range 0-14.8). Four authors reported that higher conversions rates (greater than 10%) were related to bleeding, adhesions, technical difficulty, advanced oncological diseases and the requirement of adequate oncologic margins[2,18-20].

Histopathology
Among the indications for RS of the 29 articles reviewed, malignancies were the 84% of the cases, in particular the most frequent indication was HCC (40%), followed by CRLM (21%), other metastases (14%), cholangiocarcinoma (CCC) (9%), GBC (3%) and other malignancies (13%). The median tumor size was 33 mm (range 17.8-73). Efanov *et al.*[21] emphasized that resections of greater tumors (up to 73 mm) should be performed by RS at the end of the surgeon's learning process. The median rate of R0 margin status was 95.5% (range 72.9-100).

Interestingly, Khan *et al.*[20] published an international multicenter study, in which they stratified their results for RS by tumor type (3-years overall survival was 90% for HCC, 65% for GBC and 49% for CCC) and reached comparable long-term outcomes, such as overall survival (OS) and disease free survival (DFS), to those of open and laparoscopic liver resections available in literature.

In conclusion, despite the lack of long-term results available in literature, RS is considered feasible and effective in the treatment of malignant diseases.

Short-term postoperative outcomes
ICU admission rate was described in 6 studies reporting a median frequency of 27.9% of patients requiring ICU postoperative care (range 0-83.8). Daskalaki *et al.*[12], even if reporting the 83.8% of ICU admission after RS, described a reduction in the length of the ICU stay in comparison with open surgery (2.1 days *vs.* 3.3 days, respectively).

The median rate of overall complications of the 29 reports reviewed was 18.5% (range 1.7-68.2), with a median rate of major complications (Clavien-Dindo grade 3 or greater) of 4.7% (range 0-25). Choi *et al.*[22] reported a greater frequency of overall and major complications in minor resections compared to major hepatectomies (46.7% *vs.* 42.6% and 13.3% *vs.* 9.3%, respectively), otherwise Daskalaki *et al.*[12] described a major rate of overall and major complications in major resections (31% *vs.* 15.3% and 6.8% *vs.* 2.5%, respectively).

The median LOS was 5.05 days (range 3-12). In particular, 16 studies reporting an operative time longer than 250 min revealed greater LOS, overall and major complications. Among these 16 articles, the median operative time was 294.2 min (range 251.5-491) and the corresponding median LOS was 6.4 days (range 3.9-12), overall complications rate was 9% (range 1-36) and major complications rate was 3.5 % (range 1-12).

Hospital costs for RS
Many studies documented the costs of robotic liver resections, which were higher than laparoscopy, but lower than open surgery. Daskalaki *et al.*[12] published a retrospective single center comparative study between robotic and open liver surgery, describing higher average costs for open surgery ($37,518 *vs.* $41,948) including readmissions costs, mainly because of the significant impact of ICU stay, inpatient nursing, and pharmacy costs. Similarly, Sham *et al.*[23] revealed higher perioperative costs, but significantly lower postoperative and total hospital direct costs for RS ($14,754 *vs.* $18,998), encouraging the development of RS.

Table 2. Robotic *vs*. laparoscopic liver resections

Authors	Cases		Location		Major/minor		EBL		Time		Conversion		LoS		Overall/major complications	
	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L
Chong et al.[1]	91	92	LS, Sg1	LS, Sg1	19/72	4/88	275*	212*	259*,#	217*,#	7.7	12	4.8	4.9	9.8/3.3	5.4/0
Montalti et al.[2]	36	72	PS	PS	0/36	0/72	415*	437*	306*	295*	14	9.7	6*	4.9*	19.4/11.1	19.4/6.9
Magistri et al.[6]	22	24	LS, PS	LS, PS	2/20	0/24	400	328	318*,#	211*,#	0#	16.7#	5.1	6.2	68.1/9	100/12.5
Hu et al.[13]	58	54	LLS	LLS	0/58	0/54	80*	109*	107*	96*	0	1.9	4.3	4.4	1.7/-	3.7/-
Lee et al.[14]	70	66	LS	LS	14/70	2/66	100	100	251#	215#	5.7	12.1	5	5	11.4/-	4.5/-
Lai et al.[16]	95	35	LS, PS	LS	27/75	1/34	335	336	207*,#	134*,#	4	5.7	7.3*	7.1*	14.7/1	20/-
Efanov et al.[21]	40	91	LS, PS	LS, PS	2/40	11/91	465	302	407#	296#	0	0	11#	9#	20/-	16.4/-
Fruscione et al.[24]	57	116	LS	LS	57/0	116/0	250	400	194	204	-	-	4	5	28/7	35.3/9.4
Lim et al.[25]	55	55	LS, PS	LS, PS	4/51	8/47	-	-	254	257	0	0	9	7	21.8/1.8	12.7/0
Beard et al.[26]	115	115	LS, PS	LS, PS	97/18	94/21	-	-	272*	253*	5.2#	12#	5	4	31.3/10.4	27.8/14.7
Wang et al.[31]	92	48	LS	LS	92/0	48/0	243*,#	346*,#	195*	199*	1#	10.4#	7.4*	7*	13/1	10.4/0
Spampinato et al.[36]	25	25	LS	LS	25/0	25/0	250	400	430	360	4	4	8	7	16/4	48/12
Kim et al.[37]	12	31	LLS	LLS	0/12	0/31	225	150	404#	246#	-	1	7	7	-/16.6	-/9.6
Packiam et al.[38]	11	18	LLS	LLS	0/11	0/18	30	30	175	188	0	0	4#	3#	27.2/0	0
Salloum et al.[39]	14	14	LLS	LLS	0/14	0/14	265*	121*	203*,#	140*,#	14	0	6*	6*	7.1/0	7.1/21.4
Croner et al.[40]	10	19	LS	LS	0/10	-	306	356	321	242	-	-	7	8	10/0	15.7/5.2
Ji et al.[41]	13	20	LS, Sg1	LS	9/4	4/16	280	350	338	130	0	10	6.7	5.2	7.7/-	10/-
Wu et al.[42]	52	69	LS	LS	20/52	10/69	325°,*,#	173°,*,#	380°,#	227°,*,#	5°	12°	7.9°	7.2°	5.7/0°	5.7/-°
Troisi et al.[43]	40	223	LS, PS	LS, PS	0/40	82/223	330#	174#	271	262	20	7.6	6.1	5.9	12.5/10	12.5/8.9
Tsung et al.[44]	57	114	LS	LS	21/36	42/72	200	100	253#	198#	7	8.8	4	4	19.2/1.7	25.4/0.8
Tranchart et al.[45]	28	28	LS, PS	LS, PS	0/28	0/28	200	150	210#	176#	14	7.1	6	5.5	17.8/10.7	17.8/10.7
Berber et al.[46]	9	23	LLS	LLS	0/9	0/12	136*	155*	258*	234*	1	0	-	-	11/-	17/-
Yu et al.[47]	13	17	LS	LS	3/10	11/6	388	343	291	241	0	0	7.8*	9.5*	0	11.7/-
Zeng et al.[48]	3	5	LS	LS	0/3	0/5	316*	290*	370*	249*	0	20	3	5	-	-
Lin et al.[49]	25	11	LS	LS	3/25	2/11	271	295	319	315	-	-	7.5	7	24/-	27.2/-

In case of PSM, only its data were reported. R: robotic surgery; L: laparoscopic surgery. °: referred to the sub-group of HCC. Cases: number of patients. Lesions location: PS:postero-superior segments; LS: laparoscopic segments different from the postero-superiors; LLS: left-lateral sectionectomy. Major/minor resections: number of major/minor, according to the description of the authors or calculated from the data supplied. EBL: milliliters (median/*mean). Operative time: minutes (median/*mean). Conversion rate: percentage of procedures converted to open surgery. LoS: days (median/*mean). Overall/major complications: percentage of all complications/major complications. Statistically significant results (*P*-value < 0.05) are expressed "#", if reported in the articles. "-": not reported

Robotic *vs*. laparoscopic liver surgery

Twenty-five comparative studies between robotic and laparoscopic liver surgery, including 1,043 cases (range 3-115) and 1,385 cases (range 5-223) respectively, were reviewed [Table 2]. These reports were published from 2010 to 2020. All of them were retrospective and 5 were propensity score matching studies (PSM). In case of PSM only results of the matchings were considered.

Left lateral sectionectomy

Left lateral sectionectomy (LLS) is currently performed with laparoscopy as a standard of care. Five studies focused on robotic and laparoscopic LLS, including 106 (range 9-58) and 206 (range 18-80) cases, respectively. Most of the articles reported similar perioperative outcomes between laparoscopy and RS. Many authors concluded that laparoscopic LLS remains the gold standard, since RS did not add any significant benefit, but increased the costs[13,37-39]. However, Hu et al.[13] established that RS could be the best choice to treat complex cases of LLS (tumor size > 10 cm in diameter, proximity of the tumor to major vessels, BMI > 30 kg/m^2, combined lymphadenectomy or choledochoscopy, huge left lateral section embedded in splenic fossa), reporting significantly lower EBL than in laparoscopy for these cases (131.9 mL *vs*. 320.8 mL, respectively).

Other types of resection
Among the 25 articles reviewed, the numbers of major and minor robotic resections included were 395 and 694 (63.7% and 36.3%) respectively, while laparoscopic cases were 460 and 1,002 (68.5% and 31.5%), respectively.

Three papers focused on only major hepatectomies (174 robotic *vs*. 189 laparoscopic cases). Among these, Fruscione *et al*.[24] revealed that robotic technical advantages could improve surgical outcomes in comparison with laparoscopy, reducing postoperative ICU admissions (43.9% *vs*. 61.2%) and 90-day readmissions (7% *vs*. 28.5%), with a similar median complications rate (28.1% *vs*. 35.3%) and median LOS (4 days *vs*. 5 days).

Many authors focused on the ability of RS to overcome laparoscopic drawbacks, particularly simplifying hilar and hepatocaval dissection, suturing and anastomosis, precise vessel dissection or advanced sewing. However, the numbers of complex parenchymal sparing resections involving postero-superior segments or caudate lobe were similar for RS and laparoscopy, 112 (10.7%) *vs*. 235 (16.9%), respectively.

In complex cases many comparative studies demonstrated similar safety, feasibility and postoperative outcomes, but RS was preferred over laparoscopy, especially when several and multiplanar transection lines were necessary, resulting in safe surgical margins and increasing the rate of MIS resections[2,21,26]. In the future these advantages could encourage the choice of RS in challenging cases, otherwise not feasible by laparoscopy[40,41].

Surgery related factors
Considering the 25 articles reviewed, the median EBL for RS and laparoscopy were 261 mL *vs*. 290 mL (range 30-465 *vs*. 30-457, respectively). Only three studies reported statistically significant differences of this parameter. Wu *et al*.[42] and Troisi *et al*.[43] reported greater EBL for RS (325 mL *vs*. 173 mL and 330 mL *vs*. 174 mL, respectively), in contrast with Wang *et al*.[31] (243 mL *vs*. 346 mL).

Referring to the use of the Pringle maneuver, Montalti *et al*.[2] reported its significant use during RS compared to in laparoscopy (55.6% *vs*. 22.2%, respectively) because of the crush technique, leading to a longer inflow occlusion time and greater severity of complications, evaluated by comprehensive complication index (CCI: 34.6% *vs*. 18.4%). Conversely, Spampinato *et al*.[36] published a retrospective comparative multi-institutional study, demonstrating that RS allowed for easier management of bleeding during the transection, making the application of the Pringle maneuver less necessary and reporting a significantly higher EBL for laparoscopy compared to RS (400 mL *vs*. 250 mL, respectively).

The median operative time for RS and laparoscopy was 271 min (range 107-430) and 227 min (range 96-360), respectively. Ten studies reported statistically significant longer duration with RS compared to laparoscopy, with a mean additional time of 68 min (range 34-153)[1,6,14,16,21,37,39,42,44,45]. Spampinato *et al*.[36] specified that longer robotic operative time could be related to instrument replacement and docking time, which could be reduced by improving the training of the surgical team.

In 18 articles the median operative time was longer than 250 min for RS and/or laparoscopy. In these studies, although the frequency of minor resections (69.6% *vs*. 74.3%, respectively), EBL (293 mL *vs*. 292.5 mL, respectively), LOS (6.7 days *vs*. 6.2 days, respectively) and overall complications rates (16% *vs*. 15.7%, respectively) were similar between RS and laparoscopy, the conversion rate (5% *vs*. 9.25%, respectively) was lower for RS. These results suggest that RS could increase MIS approach also in complex cases requiring longer operative time.

The reported use of hand-port in RS is lower than in laparoscopy. The reason for this observation could be the distance of the first surgeon from the patient and from the operative field that is mainly occupied by the robotic arms. Moreover, the second surgeon at the operative table could not have enough surgical skills to manage unexpected events. This statement could explain also the lower rate of conversion to hybrid robotic procedures in case of unexpected events. However, many studies reported an easier robotic management of adhesions and major intraoperative complications as bleeding than in laparoscopy, that could explain the lower rate of conversion to open surgery for RS.

The median rates of conversion for RS and laparoscopy were 4% *vs.* 7.35% (both ranges 0-20). Among the 25 comparative articles reviewed, 4 papers reported a statistically significant higher conversion rate for laparoscopy in comparison with RS[6,26,31], while the other authors did not reach statistically significant results for this variable. Only Troisi *et al.*[43] found a higher conversion rate for RS compared to laparoscopic surgery (20% *vs.* 7.6%, P = 0.034) but, considering only resections of postero-superior segments, they showed that RS provided a lower conversion rate (20% *vs.* 35.3%, P = 0.38).

Postoperative outcomes
The median rates of overall robotic and laparoscopic complications were 17.7% *vs.* 37.6% (ranges 5.7-68.1 *vs.* 27.2-48), respectively. The median rates of major complications were 2.5% *vs.* 8.9% (ranges 0-16.6 *vs.* 0-21.4), respectively.

The median LOS for RS and laparoscopy were 6 days *vs.* 5.95 days (ranges 3-11 *vs.* 3-9.5). Only Efanov *et al.*[21] and Packiam *et al.*[38] reported a statistically significant longer hospital stay for RS, mainly caused by postoperative complications and ICU stay.

Comparison of costs
Many authors confirmed the major costs of robotic resections, although the annual service fees could be cushioned by the utilization of the robot in other surgical specialties at the same institution. Kim *et al.*[37] observed that robotic LLS showed higher costs ($8,183 *vs.* $5,190) and longer operative time. Salloum *et al.*[39] suggested that robotic LLS did not add additional advantages in comparison with laparoscopic outcomes. Furthermore, while perioperative costs were higher in the robotic group, total costs were similar in comparison with laparoscopy (€5,522 *vs.* €6,035). Berber *et al.*[46] calculated a general addition of $500 per case for the robotic equipment. Ji *et al.*[41] considered RS not routinely applicable, since its higher costs in comparison with laparoscopy ($12,046 *vs.* $7,618). Packiam *et al.*[38] performed a cost analysis differentiating direct and indirect costs of RS. Only robotic indirect costs were significantly higher, adding $1,423 per case ($6,553 *vs.* $4,408). However, Yu *et al.*[47] concluded that RS could really increase in near future, overcoming the drawbacks represented by the major costs ($11,475 *vs.* $6,762) and the absence of transection tools equivalent to those available in laparoscopy.

Robotic surgery in specific malignant diseases
The majority of the publications in the literature report cumulative results, without differentiation between benign and malignant diseases. However, in future probably more specific analyses of RS outcomes for each of the most relevant hepatobiliary malignancies could help in the definition of the standard of care for each one.

Hepatocellular carcinoma
Robotic resections for HCC are feasible, safe, and demonstrated adequate oncologic outcomes. Six retrospective papers, including 294 patients, analyzed the results of RS for HCC [Table 3].

In this field the superiority of robotic MIS over open surgery was confirmed by Chen *et al.*[28] by a PSM study. Even in challenging major resections, robotic approach showed longer operative time, but shorter

Table 3. Robotic surgery for hepatocellular carcinoma

Authors	Cases	Age	Location	Major/minor	EBL	Time	Conversion	Cirrhosis	R0	LoS	Overall/major complications	DFS/OS
Magistri *et al.*[6]	22	60.8	LS, PS	2/20	400	318*	0	68	95	5.1	68/9	-
Lai *et al.*[16]	95	62.1	LS, PS	27/75	335	207	4	84	96	7.3*	14/1	5-year: 42/65
Lim *et al.*[25]	42	-	-	-	-	-	0	-	97	-	-	3-year: 64/98
Chen *et al.*[28]	81	-	-	34/47	282	343	-	46	97	7.5	5/0	3-year: 72/93
Wu *et al.*[42]	38	60.9	LS	-	-	380	5	-	-	7.9	8/-	-
Han *et al.*[50]	16	54.5	LS	10/16	389	285	0	53	100	8.4	-	-

Cases: number of patients. Lesions' location: PS: postero-superior segments; LS: laparoscopic segments different from the postero-superiors. OS: overall survival; DFS: disease free survival. Major/minor resections: number of major/minor, according to the description of the authors or calculated from the data supplied. EBL: milliliters (median/*mean). Operative time: minutes (median/*mean). Conversion rate: percentage of procedures converted to open surgery. R0: percentage of negative margin status. LoS: days (median/*mean). Overall/major complications: percentage of all complications/major complications. DFS and OS: percentage at 3-/5-year. "-": not reported

LOS, improved patients' pain control, not compromising oncologic outcomes and reaching comparable 3-years DFS (72.2% *vs.* 58.0%) and 3-years OS (92.6% *vs.* 93.7%). Magistri *et al.*[6] and Lai *et al.*[16] reported less minor robotic postoperative complications, such as pleural effusion, thanks to gentler manipulation of the diaphragm, especially in the case of lesions located in postero-superior segments. In addition, RS allowed lower rates of conversion, a greater number of resections involving the postero-superior segments, and resections of slightly larger tumors, that could explain the higher rate of major hepatectomies. Lai *et al.*[16] did not find significant differences between robotic and laparoscopic oncologic outcomes (5-years OS: 65% *vs.* 48%, respectively), morbidity and mortality. The authors concluded that robotic MIS was a valid alternative treatment for HCC in selected patients and in the hands of surgeons expert in laparoscopic and robotic liver surgery, following the principles of open liver surgery.

Likewise, Han *et al.*[50] revealed the safety and feasibility of the robotic approach to complex procedures and anatomical liver resections, and thus the superiority of minimally invasive liver surgery in terms of EBL, complication rate, LOS and risk of ascites, maintaining DFS and OS similar to open surgery.

Gallbladder cancer
RS seems particularly advantageous in the treatment of GBC, overcoming the difficulties related to the laparoscopic approach. Focusing on this field, 4 articles including 51 patients were reviewed [Table 4]. Zeng *et al.*[48] demonstrated safety and feasibility of both robotic and laparoscopic surgery. Otherwise, Goel *et al.*[19] and Byun *et al.*[51] compared results of robotic and open radical cholecystectomy. They achieved similar results between the two approaches, reaching no significant differences in operative time, EBL and number of retrieved lymph nodes, with a reduction of LOS. Likewise, Shen *et al.*[52] confirmed the feasibility of a complete robotic lymphadenectomy of the hepatic artery, the celiac axis, the hepatoduodenal ligament and retropancreatic nodes, in contrast with laparoscopy. In addition, robotic approach could reduce the risk of major iatrogenic injuries and major bleeding could be more easily managed[51,52].

In conclusion, in selected cases RS for GBC is considered safe, feasible and effective, even during the initial learning curve, allowing sufficient lymph node dissection and enhancing recovery[19,51,52].

Hilar cholangiocarcinoma
Even if the advantages of the robotic technique for procedures that require extreme precision and microanastomosis are clear, the scientific literature is lacking in reports about robotic treatment of this disease. Probably further implementation in surgeon expertise and robotic tools are necessary to reach encouraging results that could increase its use. Two articles were selected and their data tabulated [Table 5].

Li *et al.*[17] highlighted the feasibility of 48 robotic resections for Bismuth-Corlette type I, II or III hilar cholangiocarcinoma. The authors considered RS a valid alternative to open surgery in selected cases,

Table 4. Robotic surgery for gallbladder cancer

Authors	Cases	Age	EBL	Time	Conversion	Lymph nodes	Extension	R0	LoS	Overall/major complications
Goel et al.[19]	27	54	200	295	14.8	10/-	pT2-3	100	4	3.7/3.7
Zeng et al.[48]	3	-	316*	370*	0	6.3/-	pT2-3	-	3	-
Byun et al.[51]	16	64.3	295	198.3*	-	7.2/3	-	100	7	6.3/6.3
Shen et al.[52]	5	57.4	210*	200*	0	9/1,3	-	-	7.4*	0

Cases: number of patients. Major/minor resections: number of major/minor, according to the description of the authors or calculated from the data supplied. EBL: milliliters (median/*mean). Operative time: minutes (median/*mean). Conversion rate: percentage of procedures converted to open surgery. Lymph nodes: mean number of nodes obtained/mean number of positive nodes. R0: percentage of negative margin status. LoS: days (median/*mean). Overall/major complications: percentage of all complications/major complications. "-": not reported

Table 5. Robotic surgery for hilar cholangiocarcinoma

Authors	Cases	Age	Pre-op. procedures	Type of resection	EBL	Operative time	Conversion	R0	LoS	Overall/major complications	Biliary leak
Li et al.[17]	48	62.4	PTBD 41.7	RH/LH + Sg1	150	276	-	72.9	9	58.3/10.4	4.2
Xu et al.[53]	10	54	PVE 10, PTBD 60	LH/RH + Sg1 (9) ERH (1)	1360	703	0	-	16	90/30	40

Cases: number of patients. PTBD: percentage of percutaneous trans-hepatic biliary drainage; PVE: percentage of portal vein embolization; RH/LH: right/left hepatectomy; ERH: number of extended right hepatectomies; EBL: milliliters (median/*mean). Operative time: minutes (median/*mean). Conversion rate: percentage of procedures converted to open surgery. R0: percentage of negative margin status. LoS: days (median/*mean). Overall/major complications: percentage of all complications/major complications. Biliary leak: percentage. "-": not reported

allowing lymphadenectomy of groups 7, 8, 9, 12 and 13. However, they did not report details about the extension of hepatectomies for each tumor stage and the rates of conversion to open surgery. Conversely, Xu et al.[53] evaluated their results for 10 patients of fully robotic-assisted radical resection for hCCC. The authors demonstrated that this procedure is technically achievable in selected patients by expert surgeons, but without superior results to open surgery. In fact, they observed technical limitations in robotic liver mobilization and exposure, longer operative time and massive EBL, consequently increased morbidity, higher costs and poor long-term outcomes with greater rate of peritoneum implantation and multisite metastases.

Colorectal liver metastases
Many hepatobiliary surgeons encouraged the robotic approach to CRLM, achieving good surgical and oncological outcomes. Seven articles were reviewed, including 242 patients [Table 6]. Beard et al.[26] focused their PSM on RS for CRLM and considered it feasible and safe, being perioperative and long-term oncologic outcomes largely comparable to laparoscopy.

Araujo et al.[54] and Troisi et al.[43] demonstrated feasibility of non-anatomical robotic resections of lesions located in postero-superior segments, simplifying parenchymal sparing resections, not affecting the oncologic outcomes, reducing the necessity of major hepatectomies and overcoming laparoscopic drawbacks.

Fifty-four simultaneous resections of the primary tumor and liver metastases were included. In these cases, RS added additional safety and effectiveness in the management of multiple metastases, improving short-term outcomes such as EBL, bowel function return time and LOS, with the exception of operative time, reaching excellent R0 resection rates[34,55]. Even in selected cases requiring major liver resections, robotic surgery gained acceptable morbidity[56]. In addition, it is worth considering that robotic total mesorectal excision demonstrated better preservation of urinary and sexual functions, low conversion rates and favorable morbidity[49].

Table 6. Robotic surgery for colorectal liver metastases

First Author	Cases	Age	Location	Major/minor	Simultaneous	EBL	Time	Conversion	R0	LoS	Overall/major complications	DFS/OS
Guerra *et al.*[18]	59	64	LS, PS	4/78	4	200	210	12	92	6.7	27/5	3-year: 41.9/66.1
Beard *et al.*[26]	115	61	LS, PS	97/18	-	-	272*	5.2	73.7	5	31.3/10.4	5-year: 38/61
Guadagni *et al.*[34]	20	66	LS	0/20	3	250*	198*	0	100	4.7	25/0	3-year: 35.8/-
Lin *et al.*[49]	25	58.5	LS	3/22	25	271	319	-	100	7.5	24/-	-
Araujo *et al.*[54]	5	59	PS	0/5	-	160*	294*	0	100	4	20/0	-
Dwyer *et al.*[55]	6	59.3	-	0/6	6	316	401	0	100	4.5	33.3/-	-
Navarro *et al.*[56]	12	59	LS, Sg1	4/8	16	274	449	0	100	12	41/16.6	-

Cases: number of patients. Lesions' location: PS: postero-superior segments; LS: laparoscopic segments different from the postero-superiors. Major/minor resections: number of major/minor, according to the description of the Authors or calculated from the data supplied. Simultaneous: resection of the primary and secondary tumors simultaneously. EBL: milliliters (median/*mean). Operative time: minutes (median/*mean). Conversion rate: percentage of procedures converted to open surgery. R0: percentage of negative margin status. LoS: days (median/*mean). Overall/major complications: percentage of all complications/major complications. DFS and OS: percentage at 3-/5-year. "-": not reported

In conclusion, these outcomes could support the use of RS, despite the high operative time and costs.

CONCLUSION

In the field of hepatobiliary surgery, use of the robotic approach is promising, but not standardized yet. International and multicenter studies are limited, only few publications reported long-term outcomes and no randomized trials are available in literature. In the current literature many authors attempted to reach definitive conclusions about the use of RS publishing many reviews/meta-analyses. In general, almost all of these studies found RS as safe and effective with acceptable morbidity in the treatment of liver malignancies as for laparoscopy[7,57-59]. Furthermore many authors agreed with the necessity of specific training in RS, the high costs and the usefulness of RS in complex cases, such as cirrhotic patients and in complex surgical procedures including microsuturing, biliary dissection, and bilio-enteric anastomosis[59,60]. However many results of RS are still discordant, mainly in short-term outcomes, and no studies reported definitive indications and contraindications of RS because of the lack of randomized control trials. The comparison among open, laparoscopic, and robotic liver resections demonstrated that the robotic approach achieved similar results to other MIS techniques, enhancing patients' recovery after surgery.

The majority of the studies reported single center initial experiences and considered the robotic learning curve shorter than the laparoscopic one, especially for surgeons with advanced skills in open liver surgery[21,22,29,33]. Efanov *et al.*[21] established that 8-10 robotic procedures can be adequate to significantly increase the surgeons' experience and the ability to perform difficult procedures.

Choi *et al.*[22] reported results from single center and single surgeon's activity, emphasizing the usefulness of high experience on open liver surgery to approach the robotic resections, making safe and feasible all types of anatomic liver resections, even more complex ones, such as staged hepatectomy and living donor right hepatectomy. Ceccarelli *et al.*[33], describing their robotic learning curve program organized in a network between high and low volume centers, demonstrated that this strategy provides a proper standard of care without the need of reaching referral centers for the patients, even in particularly complex cases. In addition, this protocol can improve surgical skills, shortening the learning curve.

Interestingly, Lai *et al.*[61] reviewed the learning curves of robotic and laparoscopic hepatectomy and concluded that a qualified robotic surgeon should have great knowledge of liver anatomy, enough experience in open liver surgery and in the management of its major complications and a good training in both laparoscopic and robotic surgery.

In conclusion, in the era of MIS in which surgical innovations are increasing, even if the younger surgeons are more confident with MIS, both open and laparoscopic surgical experiences are necessary in order to shorten the learning curve of robotic liver surgery and all the surgeons should receive specific training for RS.

Even though robotic liver surgery allows attainment of excellent oncologic results with adequate R0 margins, long-term outcomes are still lacking, probably because of the recent introduction of this technique.

Regarding the type of liver resection, robotic LLS is considered inappropriate in comparison with the laparoscopic one, which is actually the standard of care. In fact, while perioperative outcomes are similar, costs are markedly higher for RS. On the contrary, complex cases could take advantages from RS, thus increasing the rate of MIS.

Even for other type of resections, the results available in the current literature encourage the use of robotic surgery in complex cases, for example for lesions located in postero-superior segments. Furthermore, many studies reported easier management of major intraoperative complications, such as bleeding, that could explain the lower rate of conversion compared with laparoscopy.

Among the comparative studies between MIS techniques, many of them reported a greater number of major resections for robotic surgery. Some authors explained these results with the reduced difficulty of robotic major hepatectomies in comparison with laparoscopy, allowing a potential increase of MIS in more complex cases[24,40,41].

One of the most relevant drawbacks of robotic surgery remain higher costs. Almost all the comparative studies confirmed robotic perioperative higher costs with reduced postoperative ones[23]. Even for this reason, many authors encouraged the use of RS only in complex cases.

It is possible that the increasing spread of robotic surgery and the introduction of new robotic platforms with industry competition could lead to a consistent reduction of these costs.

Regarding the application of the robotic approach in specific diseases, RS for HCC and liver metastases achieved good results, allowing parenchymal sparing resections, even in difficult locations.

Furthermore, the robotic approach to biliary tumors seems to be the most promising application of robotic surgery, because of the need for extensive lymph node dissection and of bilio-enteric anastomoses. Currently, there are discordant opinions regarding hCCC, whereas robotic surgery for GBC can add relevant benefits, increasing the rate of MIS without compromising oncologic results.

In conclusion, different techniques should be tailored to each patient, applying MIS when possible, particularly in cirrhotic patients and in the context of liver transplantation[15,34]. Thus, in a modern hepatobiliary center, both open surgery and MIS should be provided, including the robotic technique, in order to safely deal with different liver diseases requiring complex procedures[6].

In the future the technological innovation could lead to more complete, less expensive and smaller robotic systems with additional devices or software for RS, that could really change the actual scenario of MIS overcoming many of the drawbacks of RS. For example, it could become possible to approach the operation without the second surgeon, the equipment could be smaller, the docking could be easier and quicker and costs reduced thanks to the market competition.

Although a lot of hepatobiliary centers worldwide are already experienced in robotic liver surgery, more and larger studies are necessary to define its real benefits compared with laparoscopy, in order to standardize patient selection criteria and its use.

DECLARATIONS

Authors' contributions
Designed and performed the research: Ruzzenente A, Alaimo L
Collected the data: Conci S, Bagante F
Analyzed the data: Campagnaro T, Pedrazzani C
Supervised the work: Ruzzenente A, Guglielmi A
Wrote and finally approved the manuscript: Ruzzenente A, Alaimo L, Conci S, Bagante F, Campagnaro T, Pedrazzani C, Guglielmi A

Availability of data and materials
A search of the current literature on robotic liver surgery was conducted in PubMed, Medline, PMC and Google Scholar databases.

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