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Robotic hepatectomy for hepatocellular carcinoma: a clinical review

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ABSTRACT

The robotic surgical system was developed to overcome the disadvantages of conventional laparoscopic surgery. The use of robots in liver surgery was not well evaluated. This article aimed at reviewing robotic partial hepatectomy to conventional laparoscopic or open partial hepatectomy in terms of perioperative, oncologic, and healthcare costs for hepatocellular carcinoma (HCC). Studies were identified by searching MEDLINE and PubMed databases for articles from January 2004 to June 2017 using the keywords "laparoscopic hepatectomy", "robotic surgery", "robotic hepatectomy", and "hepatocellular carcinoma". Case reports were not included. The open conversion rate, overall morbidity rate, and mortality rate of robotic partial hepatectomy were reported as 0-14.3%, 0-27%, and 0-3%, respectively. Although little data regarding robotic approach for HCC have been reported, it appears to be better than open approach, particularly blood loss and hospital stay, and similar to conventional laparoscopic approach in terms of short term outcomes. The oncological outcomes were comparable to open or laparoscopic approach. Well-known advantages of the robotic system allow resection of tumor location over posterior and superior segments or major hepatectomy with more ease. The main disadvantage of robotic approach was its high cost. In conclusion, oncological data from homogenous series of HCC after robotic partial hepatectomy was needed. Robotic approach was safe to be an alternative option of minimally invasive hepatectomy for HCC. Its future implementation will depend on the advantages that it can provide over open or conventional laparoscopy approach.

INTRODUCTION

The introduction of minimally invasive surgery (MIS) has revolutionized surgical practice in the past 3 decades. MIS benefits patients in terms of better pain control, shorter hospital stay, earlier recovery, and better cosmesis [Table 1]. Traditionally, liver surgery is considered as one of the most challenging surgeries among the abdominal procedures. Its MIS development is also lag behind other gastrointestinal organs' development. These advanced techniques also require highly experienced laparoscopic skills. Increasing understanding of liver anatomy and advancements in technology have facilitated the development of MIS approach of hepatectomy[1,2]. Two international expert consensus conferences on laparoscopic partial hepatectomy were held in Louisville, KY, USA, in 2008 and in Morioka, Japan,

Quick Response Code:

Table 1: Potential advantages of MIS approach of hepatectomy

Operation	Recovery
Improved visualization Reduced blood loss Reduced blood transfusion requirement Less intra-abdominal adhesion formation	Less postoperative pain Earlier mobilization Improved perioperative lung function Fewer wound complications Reduced perioperative immune suppression Improved cosmetic outcome Shorter recovery time Shorter hospital stay Decreased ascites in patients with portal hypertension

MIS: minimally invasive surgery

in 2014, respectively[3,4]. The jury in the second consensus meeting concluded that minor laparoscopic hepatectomy should be a standard practice, and major laparoscopic hepatectomy is still in exploration phase. Continued cautious introduction of laparoscopic major hepatectomy was recommended. In a recent review, over 9,000 cases of laparoscopic hepatectomies were performed worldwide, and 65% of cases were performed for malignant pathologies[5].

The recent introduction of robotic surgical systems has given a new face of MIS. It was developed to overcome the disadvantages of conventional laparoscopic surgery. Well-known advantages of the robotic system such as improved vision via three-dimensional view, magnification, tremor suppression, and the flexibility of the instruments have allowed precise operating techniques in a variety of procedures in general surgery. These features allow the surgeons to perform delicate tissue dissection and precise intra-corporeal suturing. The main drawback of robotic system is the associated cost.

Hepatocellular carcinoma (HCC) is the sixth most common malignancy worldwide and the most common primary liver cancer. Over 80% of cases HCC grown in a cirrhotic liver[6,7]. In view of the benefit of MIS, minimally invasive approach for HCC treatment is increasing continuously adopted[8-11]. The postoperative course after MIS approach of partial hepatectomy may also be improved in patients with liver cirrhosis because the abdominal wall is preserved, kinetics of the diaphragm is improved, collateral venous drainage is better and there is less postoperative ascites. Systematic reviews or meta-analyses suggests that laparoscopic partial hepatectomy of HCC is safe and can provide improved patient outcomes when compared to the open approach[12-14]. Herein, we review the literature to compare robotic partial hepatectomy to conventional laparoscopic or open partial hepatectomy in terms of perioperative, oncologic, and healthcare costs for HCC.

Studies were identified by searching MEDLINE and PubMed databases for articles from January 2004 to June 2017 using the keywords “laparoscopic hepatectomy”, “robotic surgery”, “robotic hepatectomy”, and “hepatocellular carcinoma”. Case reports were not included.

PERIOPERATIVE OUTCOMES

Robotic *vs.* open partial hepatectomy

Three nonrandomized comparative studies compared robotic and open partial hepatectomy[15-17]. Patriti *et al.*[15] from Italy compared outcomes between robotic partial hepatectomy (n = 19) and open (n = 69) partial hepatectomy at 2 centers for lesions in the right posterior section between January 2007 and June 2012. Matched patients undergoing robotic and open partial hepatectomy showed no significant differences in blood loss (376.3 *vs*. 457.5 mL), intraoperative transfusion rate (31.6% *vs*. 15%), postoperative transfusion rate (10.5% *vs*. 7%), mean hospital stay (6.7 *vs*. 7.9 days), overall complication rate (15.8% *vs*. 13%) and mortality rate (0% *vs*. 0%). According to the Clavien-Dindo classification, major (grades 2-4) complications were not significantly different between the 2 groups (5.3% *vs*. 1.4%). Robotic group had significantly longer mean operative time (303 *vs*. 233 min) and inflow occlusion time (75 *vs*. 29 min) compared with open group. In malignancies, tumor-free margin rates were similar in both groups (R1 resections, 10.5% *vs*. 9%). Kingham *et al.*[16] from United States compared outcomes between robotic partial hepatectomy (n = 64) during 2010-2014 and open (n = 64) partial hepatectomy during 2004-2012. In the robotic group, 41% were segmental and 34% were wedge resections. There was a 6% open conversion rate. There was a significant shorter median operating time (163 *vs*. 210 min), lower median estimated blood loss (100 *vs*. 300 mL), and shorter median hospital stay (4 *vs*. 7 days) in robotic group. The complications rates (10.9% *vs*. 14.1%) and mortality rates (3% *vs*. 1.6%) were similar in both groups. Eleven of the robotic operations were isolated resections of tumors in segments 2, 7, and 8. The resection margins of the malignant tumors were similar using both groups. Margins > 10 mm were found in 16% of robotic group and 17% of open group. Daskalaki *et al.*[17] from United States compared robotic (n = 68) and open partial hepatectomies (n = 55) during 2009-2013. There was an 8.8% open conversion rate. Mean estimated blood loss was significantly less in the robotic group (438 *vs*. 727.8 mL). Overall morbidity was significantly lower in the robotic group (22% *vs*. 40%). Clavien-Dindo

Table 2: Advantages and disadvantages of conventional laparoscopic and robotic approaches

	Conventional laparoscopic approach	Robotic approach
Advantages	Well-developed technology Less start-up cost Less maintenance cost	3-dimensional magnified view Good dexterity 7 degrees of freedom in movement Elimination of fulcrum effect Elimination of physiologic tremors Good in suturing Tele-surgery More ergonomic in working position
Disadvantages	Loss of tactile feedback Compromised dexterity Limited degrees of motion Fulcrum effect Magnification of physiologic tremors	Total absence of tactile feedback High start-up cost Very expensive in maintenance New technology with limited evidence

grade 3/4 complications were also significantly lower (4.4% *vs*. 16.3%). The length of stay in the intensive care unit (ICU) was significantly shorter for patients who underwent a robotic procedure (2.1 *vs*. 3.3 days). The mean operating time (293.4 *vs*. 256 min), 30-day mortality (0% *vs*. 1.8%) and mean hospital stay (6.8 *vs*. 9.2 days) were similar in both groups. Robotic group had less overall morbidity, ICU, and hospital stay. This translates into decreased average costs for robotic surgery. The mean total cost, including readmissions, was $37,518 for robotic approach and $41,948 for open approach.

Based on current limited nonrandomized comparative studies, robotic approach has better perioperative outcomes, particularly blood loss and hospital stay, than open approach.

Robotic *vs.* conventional laparoscopic partial hepatectomy

Traditionally, conventional laparoscopic partial hepatectomy can either be pure laparoscopic or hand-assisted laparoscopic approach. Techniques of hand-assisted laparoscopic approach has been attempted to bridge the gap between open and pure laparoscopic approach. The benefits of hand-assisted laparoscopic approach in hepatectomy are: (1) facilitation in manual retraction, which may be the best atraumatic tool; (2) feasibility in assessing margins of resection with the use of tactile sensation; (3) safety in parenchymal dissection laparoscopically; and (4) possibility of immediate hemostasis and prevents air embolism in case the hepatic vein is severed. Obviously, pure laparoscopic procedure is superior to hand-assisted approach in terms of wound pain, and cosmetic outcome as hand-assisted laparoscopic hepatectomy usually required a 6-8 cm incision for the placement of the hand-port. Another possible disadvantage of hand-assisted laparoscopic approach includes possible obstruction of the visual field by the surgeon's hand during the operation. Based on the platform of the development and experiences of conventional laparoscopic hepatectomy, robotic surgical system was developed to overcome the disadvantages of conventional laparoscopic approach and hand-assisted laparoscopic approach. When robotic system compared to conventional laparoscopic approach, the pros and cons of each approach were shown in Table 2. Robot-assisted laparoscopic partial hepatectomy was increasingly studied in recent years. Up till now, no randomized trials are available for robotic hepatectomy. All data have been reported as case series or nonrandomized comparative studies. Most data were obtained from prospectively maintained databases. Tables 3 and 4 showed the results of nonrandomized comparative studies comparing robotic and laparoscopic partial hepatectomy in patients with minor hepatectomies[18-25] and in patients with minor and major hepatectomies[26-29]. Although the perioperative outcomes seemed to be similar in both groups, the benefit of robotic approach has been shown in several studies. The potential benefits included less open conversion rate, higher proportion of major hepatectomies and easier for resection of those tumours located over superior and posterior segments[22,26,28,30-33].

Based on current nonrandomized comparative studies, robot-assisted laparoscopic partial hepatectomy appears to be similar to conventional laparoscopic approach in terms of blood loss, morbidity, mortality rate and hospital stay. Robot-assisted laparoscopic hepatectomy may have longer operation time. However, the definition of operation time was variable. Some authors refer to a "total operation time" and specify an included "robot set-up and docking time", whereas others refer to a "procedure time" with a separate "system time" (from positioning the robot over the patient to disconnection of the robot) and "dissection time" (surgeon's active time at the console); others calculate the time from "induction of anesthesia to incision" or from "incision to extubation". However, robotic approach is more expensive than laparoscopic approach.

Table 3: Nonrandomized comparative studies comparing robotic and laparoscopic minor hepatectomy

Studies	*n*	Operating time (min)	Blood loss (mL)	Conversion (%)	Complication (%)	Mortality (%)	Hospital stay (days)	R0 resection (%)	Cost
Berber *et al.*[18] (2010)	9 *vs.* 23	258.5 *vs.* 233.6	136 *vs.* 155	11.1 *vs.* 0	11 *vs.* 17	\	\	\	\
Packiam *et al.*[19] (2012)	11 *vs.* 18	175 *vs.* 188	30 *vs.* 30	0 *vs.* 0	27 *vs.* 0*	0 *vs.* 0	4 *vs.* 3*	\	$6,553 *vs.* $4,408*
Lai *et al.*[20] (2013)	33 *vs.* 33	202.7 *vs.* 133.4*	373.4 *vs.* 347.7	\	3 *vs.* 9	0 *vs.* 0	\	90.9 *vs.* 90.9	\
Tranchart *et al.*[21] (2014)	28 *vs.* 28	210 *vs.* 176 (median)	200 *vs.* 150	14.3 *vs.* 7.1	17.9 *vs.* 17.9	0 *vs.* 0	4.5 *vs.* 3	\	\
Yu *et al.*[22] (2014)	13 *vs.* 17	291.5 *vs.* 240.9*	388.5 *vs.* 342.6	0 *vs.* 0	0 *vs.* 11.8	0 *vs.* 0	7.8 *vs.* 9.5	\	$11,475 *vs.* $6,762*
Kim *et al.*[23] (2016)	12 *vs.* 31	337.4 *vs.* 216.4*	225 *vs.* 150 (median)	0 *vs.* 3.2	25 *vs.* 22.6	0 *vs.* 0	7 *vs.* 7	\	$8,183 *vs.* $5,190 *
Montalti *et al.*[24] (2016)	36 *vs.* 72	306 *vs.* 295	415 *vs.* 437	13.9 *vs.* 9.7	19.4 *vs.* 19.4	2.8 *vs.* 0	6 *vs.* 4.9	88.9 *vs.* 87.5	\
Salloum *et al.*[25] (2017)	16 *vs.* 80	190 *vs.* 162	247 *vs.* 206	13 *vs.* 3	13 *vs.* 11	0 *vs.* 1	6 *vs.* 7	100 *vs.* 98	€5,522 *vs.* €6,035

*$P < 0.05$

Table 4: Nonrandomized comparative studies comparing robotic and laparoscopic minor and major hepatectomy

Studies	*n*	Operating time (min)	Blood loss (mL)	Conversion (%)	Complication (%)	Mortality (%)	Hospital stay (days)	R0 resection (%)	Cost
Tsung *et al.*[26] (2014)	57 *vs.* 114	253 *vs.* 198.5*	200 *vs.* 100	7 *vs.* 8.8	19.3 *vs.* 26	0 *vs.* 1.8	4 *vs.* 4 (median)	95 *vs.* 92	\
Spampinato *et al.*[27] (2014)	25 *vs.* 25	430 *vs.* 360	250 *vs.* 400	4 *vs.* 4	16 *vs.* 36	0 *vs.* 4	8 *vs.* 7	100 *vs.* 91	\
Wu *et al.*[28] (2014)	38 *vs.* 41	380 *vs.* 227*	325 *vs.* 173*	5 *vs.* 12.2	8 *vs.* 10	0 *vs.* 0	7.9 *vs.* 7.2	\	\
Lee *et al.*[29] (2016)	70 *vs.* 66	251.5 *vs.* 215*	100 *vs.* 100 (median)	5.7 *vs.* 12.1	11.4 *vs.* 4.5	0 *vs.* 0	5 *vs.* 5	\	\

*$P < 0.05$

ONCOLOGICAL OUTCOMES

At present, available survival data about robotic partial hepatectomy for HCC in the literature are limited still. Difficult learning curves, adequate resection margins, tumor seeding, metastases of the wounds, and the long-term outcome are the major concerns. No port-site recurrence was reported. However, specific survival data in homogenous group of pathology was very limited. The majority of the papers included deals with patients undergoing robotic partial hepatectomy for different diseases, whereas HCC represent a variable (often small) proportion of the total. Therefore, a meaningful analysis of survival data for HCC after robotic surgery was difficult still.

Robotic *vs.* open approach for HCC

In Chen *et al.*[33], a total of 183 patients underwent robotic partial hepatectomy and 275 patients underwent open partial hepatectomy by the same surgical team between January 2012 and October 2015. Eighty-one newly diagnosed HCC cases in each group were compared under propensity score matching in a 1:1 ratio. With robotic partial hepatectomy, the conversion rate was 1.6% and the complication rate was 4.4%. The two groups had a comparable percentage of major partial hepatectomy (41.9% *vs.* 39.5%) and liver cirrhosis (45.7% *vs.* 46.9%). Compared with the open group, the robotic group required longer operating times (343 *vs.* 220 min), shorter hospital stay (7.5 *vs.* 10.1 days), and lower dosages of postoperative patient-controlled analgesia (350 *vs.* 554 ng/kg). The 3-year disease-free survival of the robotic group was comparable with that of the open group (72.2% *vs.* 58.0%), and also similar in the 3-year overall survival (92.6% *vs.* 93.7%).

Robotic *vs.* conventional laparoscopic approach for HCC

In 2013, the short-term survival outcome after robotic partial hepatectomies for 41 consecutive patients with HCC was reported by Lai *et al.*[20]. The mean operation time and blood loss was 229.4 min and 412.6 mL, respectively. The R0 resection rate was 93%. The hospital mortality and morbidity rates were 0% and 7.1%, respectively. The mean hospital stay was 6.2 days. The 2-year overall and disease-free survival rates were 94% and 74%, respectively. In the subgroup

analysis of minor hepatectomies, when compared with the conventional laparoscopic approach, the robotic group had similar blood loss (mean, 373.4 *vs*. 347.7 mL), morbidity rate (3% *vs*. 9%), mortality rate (0% *vs*. 0%), and R0 resection rate (90.9% *vs*. 90.9%). However, the robotic group had a significantly longer operative time (202.7 *vs*. 133.4 min). Recently, Lai and Tang[34] also compared the long-term oncological outcomes of robotic (n = 100) and conventional laparoscopic partial hepatectomy (n = 35) for HCC. Robotic group had a significant higher proportion of major hepatectomies (27% *vs*. 2.9%) and tumors located at or across posterosuperior segments (29% *vs*. 0%) than conventional laparoscopic group. For the perioperative outcomes, robotic group had a significant longer mean operating time (207.4 *vs*. 134.2 min). Both groups had similar blood loss (334.6 *vs*. 336 mL). There was no difference in morbidity (14% *vs*. 20%) and mortality rate (0% *vs*. 0%). Concerning oncological outcomes, there was no difference between 2 groups in R0 resection rate (96% *vs*. 91.4%), 5-year overall survival (65% *vs*. 48%), and disease-free survival (42% *vs*. 38%). Recently, Magistri *et al.*[35] also reported the short-term outcomes of patients who had underwent robotic resections (n = 22) and laparoscopic (n = 24) resections for HCC. In the robotic group, there were 6 left lateral sectionectomies, 2 right hepatectomies, and 14 minor resections, including 9 segmentectomies and 5 wedge resections. In the laparoscopic group, there were 14 segmentectomies and 10 wedge resections, but no major hepatectomies. Operating time was significantly longer in the robotic group (318 *vs*. 211 min), whereas estimated blood loss was comparable between the two groups (400 *vs*. 320 mL), with one case needed blood transfusion in each group. In the robotic group, Clavien-Dindo classes I and II complication was significantly less frequent than in the laparoscopic group (n = 13 *vs*. n = 22). During analyzing specific complications, pleural effusion was significantly less frequent in the robotic group (n = 2 *vs*. n = 10). Regarding major complications, there were no differences of incidence among the two cohorts (n = 2 *vs*. n = 3). In both the groups, one case of R1 resection was observed. They also found that robotic surgery allowed the surgeon to safely deal with liver segments that are difficult to resect in laparoscopic approach, such as segments I-VII-VIII.

CONCLUSION

Although little data regarding robotic liver surgery have been reported, it appears to be superior to open approach, particularly blood loss and hospital stay, and similar to conventional laparoscopic approach in terms of operative time, blood loss, morbidity rate, mortality rate and hospital stay. However, robotic surgery is more expensive than conventional laparoscopic approach. It should be emphasized that considering robot-assisted laparoscopic partial hepatectomy requires 4 conditions: (1) appropriate selection of patients; (2) follow the principle of open liver surgery; (3) specific expertise and training, in both liver and laparoscopic surgery; and (4) familiarization with the robotic machine and pay precaution of its potential dangers, such as visceral injury by robotic arm, total loss of tactile feedback. For the oncological outcome for robotic resection of HCC, the data are very limited. Oncological data from homogenous series of HCC after robotic partial hepatectomy was needed. Its future implementation and clinical value will depend on the advantages that it can provide over conventional laparoscopy or open surgery.

DECLARATIONS

Authors' contributions

Proposed the idea, structure, and content: E.C.H. Lai
Literature search: E.C.H. Lai, D.T.M. Chung, O.C.Y. Chan
First draft: E.C.H. Lai
Revision and final proof read: D.T.M. Chung, O.C.Y. Chan, C.N. Tang

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Conflicts of interest

There are no conflicts of interest.

Patient consent

Not applicable.

Ethics approval

Not applicable.

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