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## Surgical Oncology

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# Outcomes of robotic liver resections for colorectal liver metastases. A multi-institutional analysis of minimally invasive ultrasound-guided robotic surgery

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## ARTICLE INFO

## Keywords:

Robotic liver surgery  
Minimally invasive liver surgery  
Liver surgery  
Hepatectomy  
Colorectal liver metastasis

## ABSTRACT

**Background:** Current evidence supporting robotics to perform minimally invasive liver resection is based on single center case series reporting surgical outcomes in heterogeneous groups of patients. On the contrary, relatively scarce data specifically focusing on secondary hepatic malignancies is available. The objective of this study is to assess short- and long-term outcomes following liver resection for colorectal liver metastasis on a multi-institutional series of patients.

**Methods:** All consecutive patients undergoing robotic surgery for colorectal liver metastasis at three different tertiary hospitals over a 10-year time frame were included in this analysis. All patients received ultrasound-guided liver resection according to tumor location following the principle of parenchymal sparing surgery. Perioperative, clinicopathologic and oncological outcomes were assessed.

**Results:** A total of 59 patients underwent liver resection. There were 7 cases of conversion to open surgery. The postoperative complication rate was 27%, 5% being the rate of major morbidity. Overall, the mean postoperative hospital stay was 6 days and no mortality occurred. R0 resection was achieved for 92% of lesions. At a mean follow-up of 19 months, the 1-year and 3-year DFS was 83.5% and 41.9%, while the 1-year and 3-year OS was 90.4% and 66.1%, respectively.

**Conclusions:** Robotic liver surgery does not impair surgical outcome and oncological results in patients with liver metastases from colorectal cancer.

## 1. Introduction

Liver malignancy has been originally considered as a relative contraindication to the application of minimally invasive surgery [1–3]. Nonetheless, the last two decades have seen a dramatic implementation of minimally invasive techniques for a number of abdominal neoplasms and also minimally invasive surgery is now gaining momentum [4,5]. Particularly, some concerns regarding oncological adequacy, essentially related to the risk of positive resection margins, have now been allayed [1,4–7].

Recently, robotic surgery has penetrated in the surgical practice with the purpose of ameliorating some of the technical limitations of conventional laparoscopy. Some hypothetical advantages related to the

use of the robot in minimally invasive liver surgery are still to be defined, although several reports suggest some benefits in the management of complex cases such as iatrogenic injuries of the bile duct, bilioenteric reconstruction, hepatocaval dissection, or complex dissections in difficult locations [8–10].

Despite the availability of several reports on robotic liver surgery [2,9–14], so far there is a relative paucity of data pertaining to homogeneous case series, with particular lack of oncological outcomes [13]. Herein we present our multicentric study on a consecutive series of patients receiving ultrasound-guided robotic resection for colorectal liver metastases (CRLM).

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## 2. Materials and methods

Following approval by each local Institution Review Board, data collected from the three centers prospective databases of patients undergoing minimally invasive liver surgery were retrospectively reviewed. Over a 10-year time frame, all consecutive patients with CRLM who were scheduled to receive robotic resection entered the study, according to an *intention to treat* principle. Each database included details about baseline data, surgical procedure, and postoperative surgical and oncological outcomes. Preoperative assessment featured three-phase computed tomography with or without magnetic resonance imaging or liver ultrasound, as needed. Indication for surgical treatment was given during a multidisciplinary conference including hepatobiliary surgeons, oncologists, gastroenterologists, radiologists, radiotherapists and pathologists in each institution. There were no specific exclusion criteria except absolute contraindication to the minimally invasive technique. A procedure-specific informed consent was obtained from each patient.

### 2.1. Surgical procedure

Surgeons with experience in both liver surgery and robotics performed all surgeries at three different institutions (three tertiary hospitals). For all procedures, a four-arm da Vinci Surgical Robot (Intuitive Surgical, Sunnyvale, CA) was used. A third generation system was employed earlier in the series and a fourth generation platform later in the series, depending on local availability.

Each intervention commenced with laparoscopic visual assessment of the abdominal cavity and liver surface. Robotic cart was docked next. An intraoperative ultrasound (IOUS) parenchymal assessment followed to confirm the number, size and exact location of metastases diagnosed preoperatively and to check for any further lesion [15].

Both anatomical and nonanatomical resections were performed following the principle of parenchyma preservation. [16 17] Where needed, ultrasound was used to confirm extemporaneously the correct line of transection. In order to control the liver inflow an extracorporeal tourniquet was used to encircle the liver pedicle and carry out the *Pringle maneuver* in selected cases [18]. Parenchyma was usually transected with the harmonic scalpel in the case of straight-line resections. The Kelly-clamp crushing technique using bipolar forceps was preferred for curved and angulated section lines and/or tumor dissection close to major vasculature. Hemostasis of small vessels was generally obtained with monopolar or bipolar cautery. To secure larger vessels or biliary ducts on the transection line, we used hemostatic clips or selective manual (robot-sewn) ligatures. Endostaplers were usually used to divide major hepatic veins. The specimen was generally extracted through the umbilical port or via a Pfannenstiel incision. A suction drainage was routinely left in place. A final ultrasound evaluation was performed on both the residual liver and the specimen in order to verify that radical excision has been effective.

Intraoperative blood losses were estimated by visual assessment of graduated suction canisters. Operative times were calculated as the time between pneumoperitoneum induction and closure of skin incisions, including the robot setup time. Complications were classified according to the Dindo-Clavien classification in all the three databases [19]. Major morbidity was defined as the presence of any complication of level III-V.

Patients' follow-up was conducted in a multidisciplinary manner involving surgical, medical, and oncological specialists. Any adjuvant treatment was established by consensus and any local or distant recurrence was defined radiologically, with or without pathologic confirmation.

### 2.2. Statistical analysis

Statistical analysis was performed using the Statistical Package for

**Table 1**

Preoperative characteristics of the entire series. BMI: Body Mass Index.

Patients	59
Median age	64 (43–84)
Male sex	37 (63%)
Median BMI	26 (17–38)
Prior chemotherapy treatment	14 (17%)
Multiple lesions	27 patients (46%)

the Social Sciences, v20.0 (SPSS Inc., Chicago, 134 IL, USA), with results presented in descriptive statistics as mean with standard deviation or median with range. A logistic regression was performed to ascertain the effects of preoperative status and type of surgical procedure on the relative incidence of postoperative complication and on the likelihood that patients were disease-free 1 year following surgery. Survival curves for disease free survival (DFS) and overall survival (OS) were plotted by means of the Kaplan – Meier method. Statistical significance was set at the 0.05 probability level.

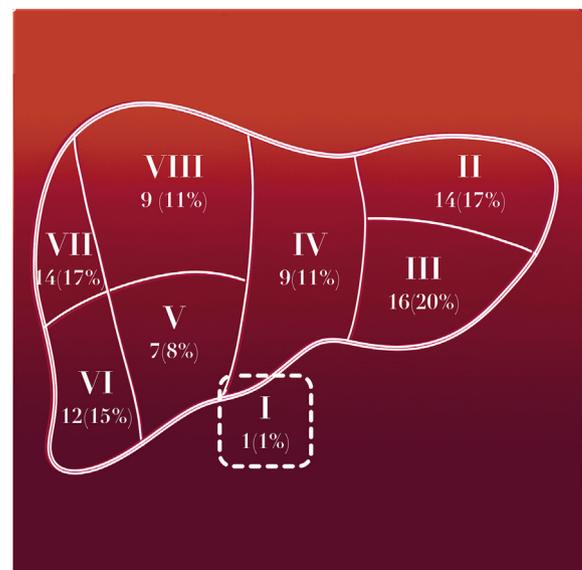
## 3. Results

Between January 2008 and February 2018, a total of 59 patients with a median age of 64 years (range 43–84) received surgery. Of these, 37 patients (63%) were male. The median BMI was 26 kg/m<sup>2</sup> (range 17–38). Preoperative patients' characteristics are given in Table 1.

Fig. 1 Summarizes the location of lesions among liver segments.

Seventeen percent of patients received chemotherapy before liver resection. Multiple lesions were excised from 27 patients (46%), while a total of 16 patients (27%) received concomitant visceral procedures, including cholecystectomy (11 patients), right colectomy (3 patients), left colectomy (1 patient), splenectomy (1 patient), ovariectomy (1 patient) and ureteroplasty (1 patient). With the exception of cholecystectomy, the rate of patients undergoing concomitant procedures was 12% (7 patients). A total of 82 liver resections were performed, which consisted of the following: 35 wedge resections, 26 segmentectomies/subsegmentectomies, 17 bisegmentectomies, 1 left hepatectomy, and three right hepatectomy. A selective Pringle maneuver was used in 18 patients (30%) during parenchymal transection.

Median estimated blood loss was 200 mL (0–1500). Overall, 6 patients received blood transfusion perioperatively. The median operative



**Fig. 1.** Representation of the location of the tumors to be resected. For each procedure, the main lesion has been considered.

time was 210 min (range 50–600). Overall, 7 surgeries were converted to an open procedure (12%). In three of these cases an intraoperative complication occurred, whereby two cases due to uncontrolled bleeding during parenchymal transection and one case of technical difficulty to divide the left hepatic vein.

During the postoperative course, a total of 16 patients (27%) experienced some complications, whereby 13 patients experienced class I – II complication, whereas 3 patients had class III – IV complications, including one case of postoperative bile leak that required radiological and endoscopic treatment and two cases of heart failure, which required intensive care management. Neither the incidence of overall complications nor that of major complications was predicted significantly by having received preoperative chemotherapy ( $p = 0.09$  and  $p = 0.9$ , respectively), the presence of multiple lesions ( $p = 0.18$ ,  $p = 0.9$ ), major hepatectomy ( $p = 0.43$ ,  $p = 1$ ) and synchronous colonic resection ( $p = 0.06$ ,  $p = 1$ ). Similarly, these variables showed no effect on the likelihood of being disease-free 1 year after hepatectomy ( $p = 0.4$ ,  $p = 0.3$ ,  $p = 0.9$ , and  $p = 0.9$ , respectively). No mortality occurred. On total, the median postoperative hospital stay was  $6.7 \pm 6.2$  days. Surgical procedures with postoperative outcomes are given in Table 2.

Median tumor size was 2.7 cm (range 0.4–13). At histopathology examination, 5 cases of microscopic resection margin involvement were noted, resulting in a 92% rate of R0 resection.

15 patients were lost at follow-up, so that long-term evaluation was available for only 44 patients. Overall, the mean follow-up period was  $19.5 \pm 15$  months. 16 cases of recurrent disease were registered in total. Of these, 10 patients had evidence of liver recurrence, while lungs and peritoneum were affected in 8 in 3 and cases, respectively. On total, 9 patients succumbed of their disease during the follow-up. The estimated 1-year and 3-year DFS was 83.5% and 41.9%, while the 1-year and 3-year OS was 90.4% and 66.1%, respectively. Oncological data are presented in Table 3.

#### 4. Discussion

Growing scientific evidence supports the specific merits of the minimally invasive methods in liver surgery [1,4–7]. The well-known advantages of laparoscopic surgery are currently offered to patients receiving liver resection for both benign and malignant diseases in several referral centers worldwide [5–7].

Robotic platforms have been proposed during the last decade with the purpose of improving the handling of challenging laparoscopic surgical procedures [8,9]. With liver surgery in particular, some evidence has suggested that the robotic system may facilitate some technically demanding procedures and ultimately widen the range of application of minimally invasive surgery [8,17,24,25]. Nonetheless, although a number of studies have shown excellent outcomes in term of

**Table 2**  
Surgical procedures with perioperative outcomes.

Patients	59
Liver procedures	82
Wedge resection	35 (42%)
Segmentectomy/Subsegmentectomy	26 (32%)
Bisegmentectomy	17 (21%)
Hemihepatectomy	4 (5%)
Concomitant procedure	27 patients (46%)
Excluding cholecystectomy	16 patients (27%)
Median blood loss	200 mL (0–1500)
Median operative time	210 min (50–600)
Conversion to celiotomy	7 (12%)
Postoperative complications	16 (27%)
Class I – II <sup>a</sup>	13 (22%)
Class III – IV <sup>a</sup>	3 (5%)
Mean postoperative hospital stay	$6.7 \pm 6.2$

<sup>a</sup> According to the Clavien – Dindo Classification of postoperative morbidity.

**Table 3**  
Oncological outcomes.

Median tumor size <sup>a</sup>	2.7 cm (range 0.4–13)
R0 resection	92%
Mean follow-up	$19.5 \pm 15$ months
Recurrent disease	16 patients
Deaths	9 patients
1-year DFS	83.5%
1-year OS	90.4%
3-year DFS	41.9%
3-year OS	66.1%

<sup>a</sup> Refers to the size of the largest tumor in patients with multiple lesions.

surgical and immediate pathological data, a few studies have evaluated oncological outcomes on the long-term [2,13]. In addition, few studies analyzed the outcomes of robotic resection for CRLMs [2,13]. At present, the largest comparison between robotic and conventional open liver resection is that presented by *Chen and colleagues* on the treatment of hepatocellular cancer [22]. Eighty-one robotic and 81 open procedures were evaluated using the propensity score matching method, with homogeneity in terms of demographics, tumor stage, rate of major resections and the presence of cirrhosis. Overall, those patients who received robotic surgeries had significantly shorter hospitalizations and lower postoperative pain, at the price of longer operative times. The subgroup analysis including only major resections favored robotics also on estimated perioperative blood losses. Interestingly, robotic surgery resulted in better disease-free survival and overall survival than open surgery, although this difference was not statistically significant ( $p = 0.06$  and  $p = 0.4$ , respectively).

Due to the scarcity of specific results in the medical literature, the aim of the present analysis was to investigate the short- and long-term clinical impact of robotic liver resection on a consecutive series of patients undergoing surgery for CLRM. Taken together, our data show that robotics is an effective option to resect CLRM providing an oncological outcome similar to that of laparoscopy and open surgery [3,4,20,21]. Pathological findings showed an adequate percentage of margin-negative resections, which was as high as 92%. The estimated 3-year DFS and OS were 41.9% and 66%, respectively. These findings are consistent with those of patients resected via conventional laparoscopy or open surgery in contemporary series [4,7,20,22,23].

Whether the robot may have actual advantages over conventional laparoscopy for liver surgery is still a matter of debate [13,17,21]. There is still scarce data comparing robotic versus conventional laparoscopic liver resection and the available evidence comes from single case-control series and few meta-analyses [2,3,12,13]. Most case series are flawed by the heterogeneity of patients (benign/malignant disease, primary/secondary malignancies) and the lack of long-term outcomes in the case of oncological conditions [9,21]. In fact, most centers have consolidated experience either in laparoscopic or in robotic liver resection. Hence, reliable comparative analyses are likely difficult to carry out.

In the largest matched analysis to date comparing robotic with laparoscopic liver resection, *Tsung et al.* included the outcomes of > 150 patients. The two groups were globally similar in terms of demographics, comorbidity and extent of resection. Overall, no significant differences were noticed with regards to general outcomes, although the rates of postoperative complications tended to be inferior in the robotic group (19% vs. 26%,  $p = 0.34$ ). Interestingly, the use of the robot permitted a higher percentage of interventions to be performed via a minimally invasive technique (93% vs. 50%), especially in the case of major resections (80% vs. 7%) [11].

*Qiu et al.* recently reported on the results of a comprehensive meta-analysis comparing robotic and laparoscopic liver resection. The authors evaluated the outcomes of more than 750 patients from 9 studies. Overall, the two techniques were similar in terms of blood losses, rate of

conversion, postoperative morbidity and mortality. Postoperative hospitalization had a trend toward a shorter hospital stay in the robotic surgery group, but this data did not reach statistical significance. The relative rate of major hepatectomies was significantly higher in the robotic group [13]. At this regard, it is interesting to note that the relative rate of major resection completed in a totally minimally invasive manner is generally low in most major studies comparing open with laparoscopic surgery [5], while the rate of major robotic hepatectomies is generally comparable to that of open surgery but significantly higher than that of laparoscopy [11,13].

Indeed, as compared to standard laparoscopy, some evidence suggests that the application of robotics may render some challenging dissections and sutures easier to perform, especially in confined surgical fields [9,10,14,16]. Furthermore, it may facilitate the management of possible intraoperative complications, even in the case of massive caval bleeding [25]. Interestingly, it seems that compared to the conventional laparoscopic approach, robotic platforms permit safer dissection and control of the hepatic veins, which are considered as most demanding maneuvers to perform minimally invasively [11,26,27]. Actually, this is particularly true when dissection posterior to the right hepatic vein or the common trunk of middle and left hepatic vein is carried out to achieve extraparenchymal venous control [11,25–28]. Beside the well-known advantages provided by robotic surgery on 3D imaging, increased range of motion and augmented surgical dexterity, one of the most interesting and innovative features of robotic technology is digitalization of the operative view [15]. The possibility to simultaneously visualize the operative field and an additional source of data, such as an intraoperative ultrasound imaging is crucial for a precise understanding of anatomy and vascularity. Moreover, the incorporation of fluorescence with indocyanine green (ICG) to the robotic system allows even more accuracy in recognition of vascular anatomy and evaluation of tissue perfusion, visualization of the biliary tree anatomy and lymph nodes identification [8,15,28,29]. Importantly, characteristic patterns of vascularization and biliary excretion of ICG may also permit to discriminate between healthy and parenchyma and tumoral tissue [29]. In this regard, it is to consider that image-guided robotic surgery is now a field in continuous and rapid evolution and it is likely that the availability of new fluorescent agents will further widen the range of application of near-infrared fluorescence in the near future [28].

All these advantages may contribute to limit the need to convert to an open procedure during robotic surgery [13,24,25]. In the present series, a total of 7 procedures (12%) were converted to open surgery. This data is consistent with that given by other reports concerning laparoscopic and robotic surgery [2,4,5,12,20,21,30]. Still, this data should be interpreted in the light of a relatively high percentage of patients receiving multiple resections and/or combined procedures (46% and 12%, respectively) in our series, as compared to that reported in most studies [4,5,21]. *Halls and colleagues* in a multicentric observational analysis including 2861 procedures have recently investigated the negative effects of conversion on the outcomes of minimally invasive liver resection. The authors focused on the risk factors for conversion and the relative effects on patient outcomes. By analyzing a total of 222 cases of conversion (nearly 8% of the entire caseload), the authors found that patients who required a conversion had significantly higher complication rate, significantly higher severity of complications and higher readmission rates. Importantly, conversion was also in connection with statistically higher mortality [30].

With reference to oncological outcomes, long-terms data concerning robotic surgery are still scarce and the present study is one of the few reporting oncological data concerning a homogeneous group of patients [2,3,12,13]. Indeed, most of the studies included in the available reviews of the literature are impaired by the fact that the reported oncological outcomes are not differentiated for specific malignancies [13]. Furthermore, most studies refer to the treatment of hepatocellular carcinoma and describe the status of surgical margins without reporting on disease free and overall survivals at the long-term [8,13]. As a

matter of fact, in the recent meta-analysis by *Qiu et al.*, the most informative data was that of *Giulianotti et al.*, which had a median follow up of 36 months, but which ultimately included only 11 patients who received surgery for CRLM [9,13]. More recently, *Tsilimigras et al.* have systematically review the available literature to investigate the safety and oncological outcomes of robotic liver surgery [31]. On total, 31 studies were included in the analysis, incorporating nearly 1150 patients. With regard to oncological outcomes, the authors found only 4 studies providing informative data. Of these, two studies analyzed the data of patients with hepatocellular cancer. Only one study reported on the DFS and OS following a mean follow-up of 14 months, but eventually included only 4 patients with CRLM. Finally, the authors included the manuscript of *Troisi et al.*, who reported on the oncological outcomes of 24 patients receiving robotic surgery for CRLM demonstrating a 1-year and 3-year DFS of 79% and 62%, respectively [21,31].

This study has several limitations, firstly due to its retrospective nature and the lack of a comparator group. Second, it is difficult to assess the role played by the specific learning curve of the procedure on the general outcomes of the series, which aggregates the experiences of three different surgical teams [21]. Further, although the median follow up was nearly 20 months, an actual oncological evaluation was not reached for each patient at the long term. Still, given the relative paucity of reliable data on the outcomes of robotic liver resection for CRLM – especially in terms of oncological evaluation – our results can significantly add to the existing literature.

Along the last years, robotic surgery has emerged as one of the most interesting and promising innovations in surgical practice. Although the diffusion of robotic platforms has been relatively rapid, their application in highly demanding procedures, such as those required by liver surgery has preceded cautiously [2,31]. Currently, the available data within the inherent literature show encouraging results, and our present analysis is one of the firsts confirming robotic surgery as a valid option to resect CRLMs competently in terms of both surgical and oncological outcomes.

## Disclosure

The authors have nothing to disclose pertaining to this paper.

## Funding

No grants or other sources of funding have been received for the drawing up of the present study.

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