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Robotic resection of hilar cholangiocarcinoma: a single institution experience

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Abstract

Aim: Hilar cholangiocarcinoma is an aggressive malignancy with a poor prognosis, for which only surgical resection offers potential cure. Because of its complex location in the porta hepatis, the standard surgical approach has been open surgery. With the gradual increase in the use of minimally invasive surgery, we aimed to describe our single institutional experience of robotic resection of hilar cholangiocarcinoma. To the best of our knowledge, this is the largest published series in North America.

Methods: Between 2016-2022, we prospectively followed all patients who underwent robotic extrahepatic biliary resection for hilar cholangiocarcinoma.

Results: Robotic resection of hilar cholangiocarcinoma was performed on 21 patients of median age 72 years, 16 (76%) of whom underwent concomitant hepatectomy. All patients initially presented with jaundice and underwent preoperative drainage. Median operative time was 458 minutes and the estimated blood loss was 150 mL. There were no intraoperative complications or conversions to open surgery. The length of stay was five days, with one readmission at 30 days. There were three postoperative complications and one postoperative mortality (at 90 days). R0 was attained in 90% (19/21) of cases and R1 in 10% (2/21). Our median follow-up time was 21 months. At the final follow-up, 15 patients were alive with no evidence of disease and six died.

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Conclusion: Robotic resection of hilar cholangiocarcinoma is safe and feasible and achieves excellent outcomes. We believe that robotic surgery will soon be an accepted approach for complex hepatobiliary resections, such as for hilar cholangiocarcinoma.

Keywords: Robotic, hilar cholangiocarcinoma, Klatskin tumor, hepatectomy, bile duct cancer

INTRODUCTION

Hilar cholangiocarcinoma (Klatskin tumor) is a rare and highly aggressive malignancy with a poor prognosis[1,2]. Surgical resection is the only potentially curative treatment modality and achieves the best long-term survival; however, hilar cholangiocarcinoma is one of the most challenging cancers to treat[3]. Many factors prejudice the treatment of this complex disease, including its critical location at the confluence of the bile duct, its aggressive tendency to involve adjacent structures, including major blood vessels, and its pattern of growth along the biliary tree, which makes it difficult to determine the extent of the disease. Additionally, resection of hilar cholangiocarcinoma requires systematic portal lymphadenectomy and complex bilioenteric reconstruction[4,5]. Given these features, a standard open approach is advocated by most hepatobiliary surgeons. Some even consider that a minimally invasive approach to hilar cholangiocarcinoma resection is contraindicated.

The advent of minimally invasive liver surgery (MLS) has marked a new era in hepatobiliary surgery. Over the past two decades, MLS has been increasingly performed and has achieved better outcomes than an open approach[6-8]. A laparoscopic approach to hilar cholangiocarcinoma has been marginally adopted and reported in small numbers, mostly from China[9,10]. Robotic liver surgery has gone one step further in that the benefits inherent in using this system have made it possible to perform both the most complex liver resections and high biliary reconstruction. Previous studies on robotic hepatectomy with biliary reconstruction for hilar cholangiocarcinoma are limited to small series and case reports; these have shown that this approach is safe and feasible[11-13]. The largest Western series reported to date included only four patients[14]. We therefore report here our single institutional experience of 21 patients who underwent robotic resection of hilar cholangiocarcinoma. To the best of our knowledge, this is the largest robotic series ever reported in the Western hemisphere. Our hypothesis was that robotic resection of hilar cholangiocarcinoma can be performed safely with excellent postoperative outcomes.

METHODS

With institutional review board (IRB) approval, from September 2016 through April 2022, we prospectively followed 21 consecutive patients who had undergone robotic extrahepatic biliary resection and reconstruction for hilar cholangiocarcinoma, with or without hepatectomy. Preoperative diagnoses of hilar cholangiocarcinoma were based on clinical findings, high-quality imaging, advanced endoscopy with cholangiography, and cholangioscopic biopsy in the majority of cases. Patients with intrahepatic cholangiocarcinoma, benign or premalignant biliary diseases, and distal cholangiocarcinoma were excluded from the study.

Patient characteristics and other clinical data collected and analyzed included age, sex, Body Mass Index (BMI), American Society of Anesthesiology (ASA) score, Childs-Pugh score, Model for End-Stage Liver Disease (MELD) score, tumor size, jaundice on presentation, preoperative biliary drainage, preoperative positive biopsy, neoadjuvant treatment, jaundice on day of surgery, operative duration, estimated blood loss (EBL), Bismuth-Corlette Classification, concomitant hepatectomy, intraoperative complications, lymph nodes removed, lymph node positivity, margin status, pathological type, postoperative complications according to the Clavien-Dindo classification, length of stay (LOS), 30-day readmission, in-hospital mortality, 90-day mortality, follow-up time, and current oncological status.

The preoperative workup included a triple phase 1-mm cut computed tomography (CT) scan of the abdomen and pelvis, chest CT, and abdominal magnetic resonance imaging (MRI) with magnetic resonance cholangiopancreatography (MRCP). This high-quality imaging is mainly performed to evaluate the blood vessels (portal vein and hepatic artery) along the porta hepatis and to assess any aberrant vasculature and/or vessel involvement. MRCP is performed to map the biliary tree, assess the extent of intrahepatic sectoral biliary obstruction, and plan reconstruction of the biliary tree after completion of resection. Future liver remnant volume was calculated on the basis of imaging findings in patients who required extended major hepatic resection. Patients with cholangitis, hyperbilirubinemia > 3 mg/dL, or who required a major hepatectomy with borderline future liver remnant volume underwent preoperative biliary drainage. In most cases, drainage was achieved by endoscopic retrograde cholangiopancreatography (ERCP) with brushing and stent placement. Many of the patients had already undergone this procedure prior to referral to our center. When available and necessary, cholangioscopy with biopsy was added. Percutaneous transhepatic cholangiography (PTC) was performed when bilirubin concentrations remained high following ERCP stenting or when ERCP was not technically feasible. In addition, every patient was clinically evaluated in terms of performance status, medical comorbidities, and cardiac and liver function.

Operative procedure

All operations were performed using the da Vinci Xi® robotic surgical system (Intuitive Surgical, Sunnyvale, CA, USA). Exclusion criteria for the robotic approach comprised hepatic artery and/or main portal vein invasion that required major vascular resection and reconstruction. Patients were placed in a supine position with both hands abducted to less than 90° on arm boards. Following the insertion of an 8-mm port through the umbilicus, the procedure commenced with diagnostic laparoscopy. After excluding peritoneal spread, an 8-mm port was placed along the right midclavicular line and a 12-mm port along the left midclavicular line, both at the level of the umbilicus. A fourth 8-mm port was placed in the left anterior axillary line. Finally, an Advanced Access Gelport® (Applied Medical, Rancho Santa Margarita, CA, USA) was placed between the right midclavicular line and umbilicus, slightly inferior to the umbilicus. The Gelport® is used by the bedside surgeon, mainly for suctioning and insertion of sutures. The incision (3-5 cm) needed for the Gelport® is also used as the extraction site for the specimen. An AirSeal® port (ConMed, Largo, FL, USA) was inserted through the Gelport® for insufflation and smoke evacuation [Figure 1]. The patient was positioned in a 15° reverse Trendelenburg and 5° right-side-up position. The da Vinci Xi® robotic surgical system was docked from the patient's right shoulder and paired with the operating table to allow for intra-operative movements of that table [Figure 2]. Next, the falciform ligament was dissected, exposing the liver surface and excluding the presence of liver metastases. The liver was retracted cranially using the fourth arm until the porta hepatis area was well exposed. Next, a meticulous and delicate dissection of the porta hepatis was started, removing all lymph nodes encountered while exposing the bile duct, portal vein, and hepatic artery. This was mostly achieved using robotic hook cautery and fenestrated bipolar forceps. The lymphadenectomy was usually started next to the common hepatic artery and celiac trunk and continued cephalad, dissecting the portal and common bile duct (CBD) lymph nodes all the way up to the hilar plate. A cholecystectomy was performed and the gallbladder retracted to the left to complete the dissection between the common hepatic duct and right hepatic artery dorsally. The duodenum was then mobilized (Kocher maneuver) to facilitate retroduodenal lymphadenectomy. The next step was transection of the distal bile duct as it enters the head of the pancreas. While awaiting frozen section analysis of the distal margins, the tumor extent was reevaluated using intraoperative cholangioscopy, viewing the intrapancreatic bile duct distally and the common bile duct/common hepatic duct/biliary bifurcation proximally. Upon confirmation of clear margins, the opening of the distal CBD was sutured to prevent

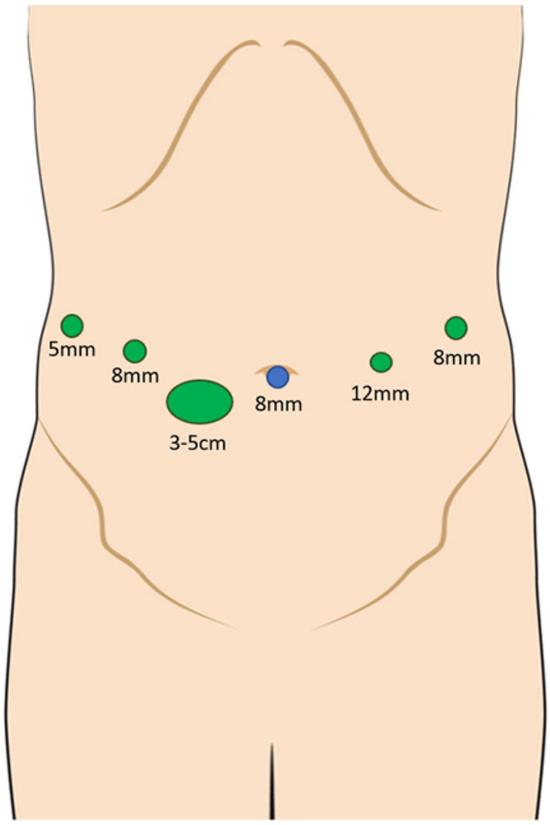

Figure 1. Port placement for robotic extrahepatic biliary resection.

retrograde pancreatic leak. Cephalad dissection was continued over the common hepatic duct towards the hilar plate, which was lowered after exposing the Laennec capsule located at the inferior margins of segments IVB/V. Next, the proximal bile duct was transected in accordance with the Bismuth-Corlette classification and intraoperative cholangioscopic findings. Concomitant hepatectomy was performed as appropriate for the type and level of tumor involvement. Technical aspects of our robotic hepatic resection procedure have previously been described in detail elsewhere[15,16]. Once the specimen had been disconnected from the future liver remnant, it was placed in an extraction bag and removed through the Gelport® incision. Biliary reconstruction was achieved using a 60-cm jejunal limb to perform a classical Roux-en-Y hepaticojejunostomy (RYHJ). A side-to-side jejunojejunostomy was completed with two 45-mm robotic blue load staplers. The common enterotomy was sutured with two 3-0 barbed sutures. Finally, an end-to-side hepaticojejunostomy was created in an antecolic fashion using two 4-0 absorbable barbed sutures, 15 or 22 cm in length, depending on the size of the bile duct. A closed suction drain was placed before closing. Depending on tumor location, major hepatectomy was sometimes necessary. For Klatskin Type 3A tumors, an anatomical right hemihepatectomy with preservation of the middle hepatic vein, including resection of the caudate process and paracaval portion of segment I, was performed. The extrahepatic biliary tree was resected en bloc with the involved right hemiliver, followed by a Roux-en-Y hepaticojejunostomy to the left hepatic duct. For Klatskins Type 3B tumors, an anatomical left hemihepatectomy with preservation of the middle hepatic vein, including resection of the Spiegel lobe and paracaval portion of segment I, was performed. The extrahepatic biliary tree was resected en bloc with the involved left hemiliver, followed by a Roux-en-Y hepaticojejunostomy to the secondary right hepatic bile ducts. In this scenario, the right anterior and right posterior hepatic ducts were joined together using a unification ductoplasty technique to enable a single biliary anastomosis. Central hepatectomy, which

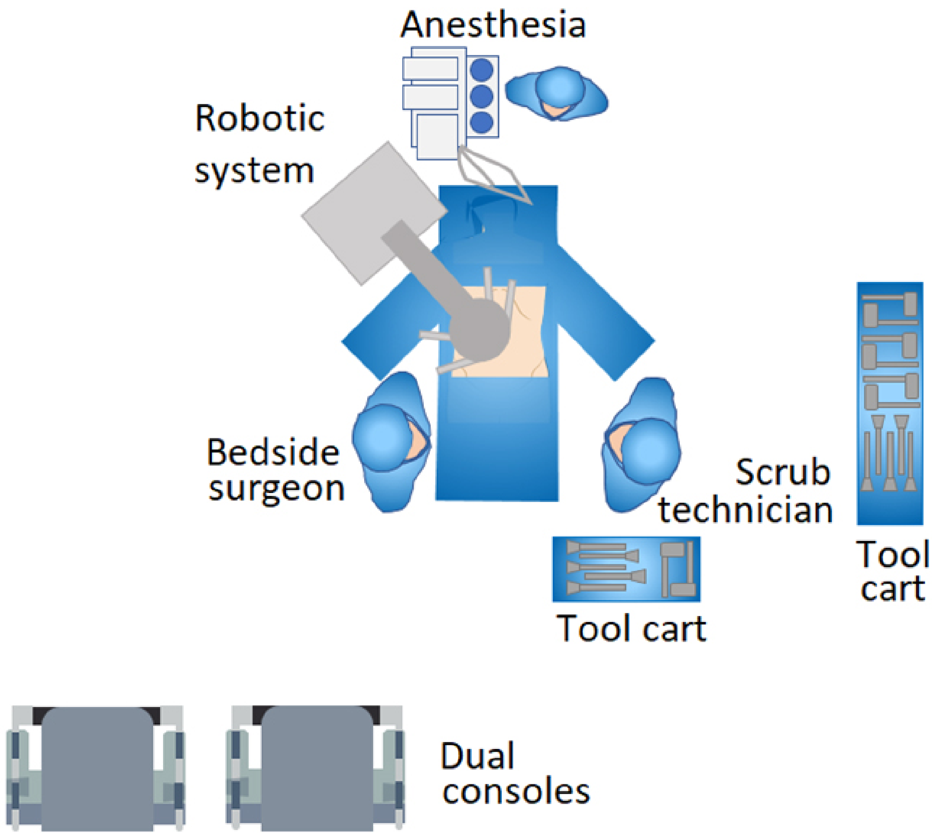

Figure 2. Operation room setup for robotic extrahepatic biliary resection.

included resection of segments 4B/5 and the paracaval portion of the caudate lobe, was only performed for Klatskin Type 2 tumors with limited involvement of the biliary bifurcation after securing negative margins on both the right and left hepatic ducts by intraoperative examination of frozen sections. This situation is much less common than typical Klatskin tumors, and in most of them, preoperative biliary endoscopy SpyGlass® (Boston Scientific Corporation, Natick, MA, USA) suggested limited tumor involvement. Supplementary video 1 attached to this manuscript depicts our surgical procedure.

Data were documented on an Excel (Microsoft) spreadsheet and analyses were carried out using GraphPad Prism 8TM software (GraphPad Software, San Diego, CA, USA). The data are presented as median (mean ± standard deviation).

RESULTS

During the study period, 21 patients underwent robotic extrahepatic biliary resection, with or without hepatectomy, for hilar cholangiocarcinoma. The median age was 72 (71 ± 8.3) years; 14 (67%) were men and seven (33%) were women. The median BMI was 25 (27 ± 5.9) kg/m^2, Child-Pugh score 5 (6 ± 1.0), and MELD score 9 (11 ± 6.0). All patients initially presented with jaundice and underwent preoperative biliary drainage; 15 (71%) patients had a stent placed by ERCP, one (5%) was stented by PTC, and five (24%) required both ERCP and PTC. Positive biopsies were obtained in 17 (81%) patients, three (24%) of whom were referred for neoadjuvant treatment before resection. On the day of operation, 13 (62%) patients had persistent, mostly mild, hyperbilirubinemia (1-3 mg/dL). Four patients had persistent hyperbilirubinemia with bilirubin > 3 mg/dL despite all drainage efforts [Table 1].

Table 1. Preoperative patient characteristics and clinical data

Variables	Number
Number of patients	21
Age (years)	72 (72 ± 8.6) [55-90]
Sex (M/W)	14M/7W
BMI (kg/m^2)	25 (27 ± 5.9) [19-40]
ASA class	3 (3 ± 0.4)
Childs-pugh score	5 (6 ± 1.0)
MELD score	9 (11 ± 6.0)
Tumor size (cm)	2 (2 ± 1.2) [0.7-3]
Jaundice at presentation	21 (100%)
Preoperative biliary drainage	21 (100%)
ERCP drainage (*n*)	15 (71%)
PTC drainage (*n*)	1 (5%)
ERCP and PTC drainage (*n*)	5 (24%)
Preoperative positive biopsy (*n*)	17 (81%)
Neoadjuvant therapy (*n*)	3 (14%)
Jaundiced on day of surgery	13 (62%)
Bilirubin 1-3 mg/dL	9 (69%)
Bilirubin > 3 mg/dL	4 (31%)

ASA: American Society of Anesthesiologists; BMI: body mass index; ERCP: endoscopic retrograde cholangiopancreatography; MELD: Model for End-Stage Liver Disease; PTC: percutaneous transhepatic cholangiography. Data in the table are presented as median (mean ± standard deviation) [range], where applicable.

According to the Bismuth classification, four patients had Type I disease, five Type II, 10 Type III, and two Type IV. Sixteen patients (76%) required concomitant hepatectomy; one underwent right hepatectomy, seven left hepatectomy, and eight central hepatectomy. Operative time was 458 (433 ± 116.9) minutes with an EBL of 150 (175 ± 123.8) mL. There were no intraoperative complications and no conversions to open surgery. Final pathological outcomes were as follows: four (5 ± 2.9) lymph nodes were examined per case, 0 (0 ± 0.4) lymph nodes were positive, R0 was attained in 90% (19/21) of cases and R1 in 10% (2/21) [Table 2].

Following stratification according to the Bismuth classification, there were no statistically significant differences between operative times for different Bismuth types ($P = 0.69$). The EBL for Bismuth Types I/II/III/IV was 275/100/150/113 mL, respectively ($P = 0.79$). The R1 resection rate was 25% (1/4) for Bismuth Type I and 20% (1/5) for Bismuth Type II. In the two cases in which R1 resection was not achieved, the margins were reported as negative on frozen section; however, the final pathological examination revealed microscopic involvement of the margins. All procedures on patients with Bismuth Types III and IV achieved clear margins [Table 3].

Overall, there were three postoperative complications. Two patients developed intra-abdominal fluid collections that required intravenous antibiotics and percutaneous drainage. One of them, a 90-year-old patient with emphysema, was discharged on postoperative Day 12 and died within 90 days of respiratory failure. Another patient developed a small pneumothorax, probably due to a central line placed preoperatively. The pneumothorax resolved spontaneously without the need for tube thoracostomy. Median LOS was 5 (6 ± 3.4) days with one readmission at 30 days. There were no in-hospital mortalities. At a median follow-up time of 21 months, 15 patients were alive with no evidence of disease and six had died [Table 4]. The median overall survival had not been reached at the time of analysis. The one-year survival rate was 78% and the three- and five-year survival rates were both 60% [Figure 3].

Table 2. Intraoperative variables

Variables	Number
Operative duration (minutes)	458 (433 ± 116.9) [279-573]
EBL (mL)	150 (175 ± 123.8) [10-450]
Bismuth-corlette classification	
Type I	4
Type II	5
Type III	10
Type IV	2
Concomitant hepatectomy	16 (76%)
Right hepatectomy	1 (6%)
Left hepatectomy	7 (44%)
Central hepatectomy	8 (50%)
Intraoperative complications (*n*)	0
Lymph nodes harvested (*n*)	4 (5 ± 2.9) [1-12]
Lymph nodes positive (*n*)	0 (0 ± 0.4) [0-2]
Margin status	
R0	19 (90%)
R1	2 (10%)
R2	0

EBL: Estimated blood loss; Data in table are presented as median (mean ± standard deviation) [range], where applicable.

Table 3. Intraoperative variables stratified by Bismuth classification

Bismuth classification	Type I *n* = 4	Type II *n* = 5	Type III *n* = 10	Type IV *n* = 2	*P*-value
Operative time (minutes)	453 (416 ± 93.0)	383 (383 ± 55.0)	518 (453 ± 158.0)	486 (486 ± 40.0)	0.69
EBL (mL)	275 (225 ± 119)	100 (180 ± 160)	150 (166 ± 125)	113 (113 ± 124)	0.79
Margin status (r0/r1/r2)	3/1/0	4/1/0	10/0/0	2/0/0	0.36
Lymph node harvested (*n*)	6 (7 ± 4.1)	3 (3 ± 2.6)	5 (5 ± 2.6)	3 (3 ± 1.4)	0.33
Lymph nodes positive (*n*)	1 (1 ± 1.0)	0 (0 ± 0.4)	0 (0 ± 0.3)	0 (0 ± 0)	0.20

EBL: Estimated blood loss; Data in table are presented as median (mean ± standard deviation), where applicable.

DISCUSSION

Hilar cholangiocarcinoma is one of the most complex malignancies to diagnose and treat. Its characteristic clinical presentation of obstructive jaundice with intrahepatic bile duct dilation usually requires preoperative drainage to resolve the cholangitis and improve hepatic function. However, unlike pancreatic head cancer or distal cholangiocarcinoma, where the drainage procedure is usually straightforward, in hilar cholangiocarcinoma, drainage can be challenging, requiring multiple biliary drains to achieve decompression and prevent the development of a cholestatic liver. In addition, it is often difficult to obtain a positive biopsy and determine the full extent of biliary involvement, this sometimes only being determined intra-operatively. The aggressive biology of this tumor is a major contributor to its complexity in that adjacent structures, such as lymph nodes and major vessels, are frequently involved, often necessitating meticulous lymph node dissection and a major liver resection, with or without vascular reconstruction. Finally, its critical location at the confluence of the bile duct, together with its propensity to grow along the biliary tree, may result in a difficult and high bilioenteric reconstruction. These complex considerations have resulted in most surgeons using a traditional open approach. Our hepatopancreatobiliary unit has gained considerable experience in robotic liver and pancreas surgery over the past six years. Having

Table 4. Postoperative variables

Variables	Number
Postoperative complications (*n*)	3
Pneumothorax	1
Intra-abdominal fluid collection	2
Clavien-dindo classification	
Grade II	1
Grade III	2
Length of stay (days)	5 (6 ± 3.4) [3-14]
30-day readmission (*n*)	1
In-hospital mortality (*n*)	0
90-day mortality	1
Follow-up time (months)	21 (22 ± 14.9) [1-63]
Current status	
Alive without disease (*n*)	15
Alive with disease (*n*)	0
Deceased (*n*)	6

Data in table are presented as median (mean ± standard deviation) [range], where applicable.

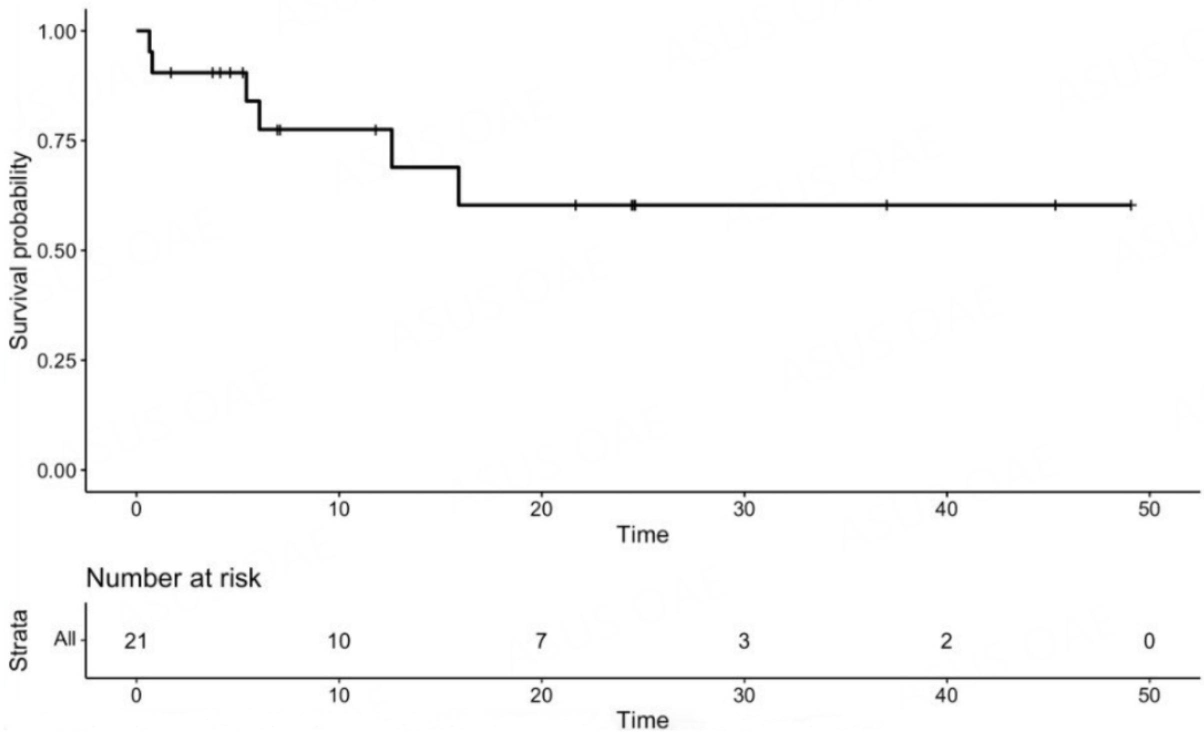

Figure 3. Kaplan-Meier overall survival curve.

extensive experience in robotic pancreatectomy enabled us to successfully implement a robotic surgical platform for biliary and hepatic surgery. We started with simple procedures such as peripheral anterolateral segmentectomy and left lateral hepatectomy, then gradually progressed to more complex procedures such as formal left hepatectomy, caudate lobe resection, and formal right hepatectomy, ultimately achieving the most challenging procedures, including robotic resection of hilar cholangiocarcinoma. To the best of our knowledge, this series of 21 patients who underwent robotic extrahepatic bile duct cancer resection with or without concomitant hepatectomy is the largest robotic series reported in the Western world so far. Our results support our hypothesis that robotic resection for hilar cholangiocarcinoma is safe and achieves excellent postoperative outcomes.

Most of our patients were men in their 70s. All patients presented with obstructive jaundice and underwent a preoperative drainage procedure, in most cases by ERCP. Preoperative biliary drainage and the best modality to use (endoscopic via ERCP *vs.* percutaneous via PTC) are well-known controversial issues in the management of hilar cholangiocarcinoma; however, preoperative biliary drainage is required prior to most resections[17]. We have chosen to utilize ERCP for the following reasons. First, our center has a highly skilled and experienced advanced endoscopy unit that is capable of successfully performing this procedure with minimal complications. Second, performing cholangiography is extremely important in clarifying the anatomy of the biliary tree and it provides better quality information than MRCP. Third, obtaining a positive biopsy is important, especially before embarking on a complex surgery with the potential for high morbidity. In recent years, the use of ERCP with cholangioscopy has resulted in significant improvement in diagnostic accuracy with minimal morbidity. We achieved positive preoperative biopsies in 81% of our cases, similar to a previous multicenter study[18]. Fourth, preoperative drainage of the future liver remnant is necessary for patients who require major hepatectomy because significant cholestasis can impair liver function and regeneration following major liver resection[19]. Despite all our drainage efforts, on the day of surgery, four patients still had bilirubin concentrations of > 3 mg/dL.

The operative time was 458 (433 ± 116.9) minutes and the EBL was 150 (175 ± 123.8) mL. Our results are superior to other studies on robotic resection of hilar cholangiocarcinoma. A previous series of 10 patients by Xu *et al.* reported an operative time of 703 ± 62 minutes with intraoperative blood loss of 1360 ± 809 mL[20]. Another small Western series by Cillio *et al.* reported a median operative time of 840 minutes with an EBL of 700 mL[14]. Poor patient selection and lack of experience in robotic surgery may have contributed to these results. A meta-analysis by Tang *et al.* showed a shorter operative time of 207-366 minutes than an open approach; however, the EBL was higher, with reported volumes being 259-1014 mL[21]. Our low blood loss can be explained by the extensive experience we have gained over some years: we have used the robotic system to perform more than 400 hepatic resections so far. The robotic platform provides better visualization with a magnifying 3D camera, tremor filtration, increased dexterity via a robotic arm with seven degrees of freedom, and a stable platform. This combination of features leads to the highest possible quality and most precise dissection, resulting in reduced blood loss. Although the operative time was longer than with open procedures, there were no intraoperative complications or conversions to an open approach. Moreover, we achieved excellent postoperative outcomes with a short hospital stay of five days, two (9.5%) major complications (Clavien-Dindo ≥ 3), and one (4.7%) postoperative mortality at 90 days. Ma *et al.* compared open *vs.* laparoscopic surgery for hilar cholangiocarcinoma and reported a hospital stay of 13.5 *vs.* 14.7 days, respectively, and a major complication rate of 14.9% *vs.* 20%, respectively[22]. A study by Wiggers *et al.* reported a postoperative 90-day mortality rate of 14%[23].

As to oncological outcomes, we achieved an R0 resection rate of 90% and a survival rate of 71% over a follow-up period of almost two years. These results are non-inferior to those of an open series on cholangiocarcinoma that reported an R0 resection rate of 41%-77%[24,25]. Of interest, a recent study of 708 cases by Mueller *et al.* defined benchmark values for surgical and oncological outcomes for hilar cholangiocarcinoma; they cited a benchmark cut-off for R0 resection of ≥ 57% and a benchmark survival rate of ≥ 61.5% at two years[26].

In summary, we here present our initial series of robotic resections of hilar cholangiocarcinoma. Our results indicate that with adequate surgical experience, this operation can be performed safely with excellent outcomes. The main limitation of this study is that it was not a comparative study: we did not compare our results with those of an open surgery control group. Another limitation was the small cohort of 21 patients, which is unsurprising given the rarity of this disease. However, this is the largest published Western cohort of patients undergoing robotic surgery for Klatskin tumors and it presents various benefits in perioperative outcomes without compromising oncological outcomes. As this technology keeps growing and advancing, we believe that the use of a robotic platform will become an alternative approach, not only for major liver operations but also for resection of hilar cholangiocarcinoma.

DECLARATIONS

Authors' contributions

Made substantial contributions to the conception and design of the study and performed data analysis and interpretation: Jacoby H, Rayman S, Ross S, Rosemurgy A, Sucandy I
Performed data acquisition and data analysis, and provided administrative, technical, and material support: Crespo K, Syblis C

Availability of data and materials

Not applicable.

Financial support and sponsorship

Not applicable.

Conflicts of interest

Ross S: Reports educational (personal fees and non-financial support) relationship with Intuitive Surgical Incorporated, outside the submitted work. All other authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

All participants were properly consented, and the study was approved by the IRB (1302427).

Consent for publication

Not applicable.

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