Robotic HPB Surgery

Building a Program

Carolijn L.M.A. Nota

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Voor mijn ouders, Margot, Irene en Sjoerd Pieter

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Robotic HPB Surgery

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opzet van een programma
(met een samenvatting in het Nederlands)

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Contents

Appendices

Chapter 1

General Introduction and Thesis Outline

Partially adapted from

Robotic Developments in Cancer Surgery

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Jeroen Hagendoorn, Yuman Fong

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General Introduction and Thesis Outline

Hepato-pancreato-biliary surgery

Hepato-pancreato-biliary (HPB) surgery comprises the entire spectrum of surgical procedures of the liver, the pancreas and the biliary system and can be highly complex. Malignancies form the most frequent indication for surgery of these structures and, at present, cancers of the HPB area contribute significantly to the entire burden of gastrointestinal cancers and cancer-related deaths. However, symptomatic benign or premalignant lesions account for a considerable amount of indications for liver and pancreatic resections as well. Treatment of these patients can consist of many therapeutic modalities including chemotherapy, surgery, radiation and/or locally ablative therapies. Nevertheless, in *all* patients who are treated with a curative intent, surgery plays an important role.

Liver resection is a very heterogeneous procedure, ranging from small wedge resections to extended resections of six or more hepatic segments. In the Netherlands, the vast majority of liver resections is performed for colorectal liver metastases.[1] In pancreatic surgery, two procedures can be identified which are most frequently performed: pancreatoduodenectomy and distal pancreatectomy. (Figure 1) Most pancreatic resections are performed for pancreatic adenocarcinoma, namely 59% in 2017.[2] Tumors originating from the biliary system (e.g. intrahepatic cholangiocarcinoma, Klatskin tumors, distal cholangiocarcinoma or gallbladder cancer) are mainly resected through/combined with liver or pancreatic resection, dependent of the location of the tumor. Surgery of the bile ducts alone forms a smaller portion of HPB surgery, less often indicated.

The history of HPB surgery and its pioneers

HPB surgery has a relatively short history and has been subject to many technical developments and anatomical insights/discoveries since the first reports describing resections of the liver and pancreas were published in the late 19th century. [3,4] Over these past 150 years HPB surgery has evolved from high-risk procedures only embarked on by surgical pioneers to routine procedures with strongly reduced mortality rates.

Over time in history, several important insights on vasculature and hepatic segmentation were gained by, amongst others, Francis Glisson (17th century, 'Glisson's capsule'), Hugo Rex and James Cantlie (19th century, 'Rex-Cantlie line'), Carl-Herman Hjortsjö and John Healey (1950's, anatomy of intrahepatic bile ducts and vascular tree) and Claude Couinaud (1954, liver segments, 'Couinaud's segments'). [5-11] Still, the applicability in liver surgery of the knowledge on hepatic segmentation was limited, since imaging techniques were limited and patients generally presented with late-stage disease. Moreover, intraoperative bleeding remained a problem and the mortality of major liver resections around that time lingered around 50%. After the introduction of ultrasound and intraoperative ultrasound around the 1980's, liver surgery rapidly developed, since surgeons could visualize biliary and vascular anatomy and start looking for tumors and perform segmental resections. In the words of French liver surgeon Henri Bismuth: individual patients could now be offered '*hépatectomie à la carte*'. [11, 12]

The following years, several techniques and devices were developed to reduce blood loss and perform safer surgery. Around 2000 a trend towards centralization of liver surgery was initiated, advocated by John Birkmeyer amongst others, and morbidity and mortality rates further decreased to where we are now: an era in which liver resection is routinely performed for various indications with low mortality rates (< 5%). [13-16]

1.1 1.2 1.3

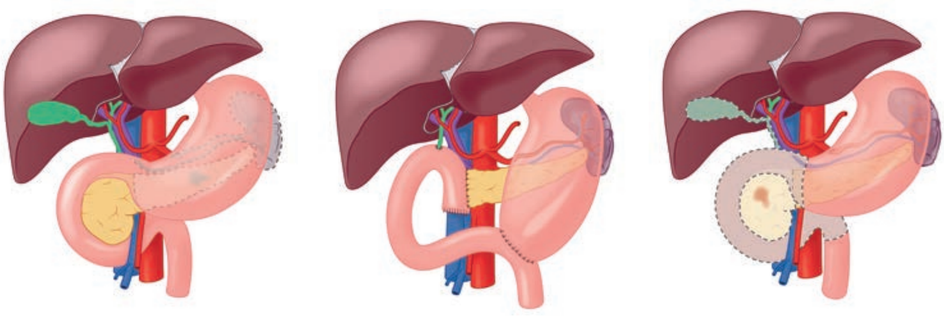

Figure 1. Schematic representation of a pancreatoduodenectomy (resection in 1.1 and reconstruction in 1.2) and a distal pancreatectomy (1.3). The dashed lines indicate the resected structures.

As for the first elective liver resection, pancreatic resection origins from the late 19th century as well when American surgeon William Steward Halsted performed the first successful resection of a peri-ampullary malignancy.[3] The procedure was further developed during the 20th century. The pancreato-duodenectomy ('Whipple' procedure) still bears the name of the surgeon who performed the first one-stage procedure resecting the complete duodenum and pancreatic head in 1940: American surgeon Allen Oldfather Whipple. Although Whipple 'just' performed 37 pancreatoduodenectomies during his lifetime, he laid the foundation for further developments in resections of the pancreas and peri-ampullary region. Nowadays, pancreatic resections are performed routinely and perioperative mortality rates have been brought down to 3-4%. [17, 18]

Minimally invasive HPB surgery

Traditionally, resections of liver and pancreatic tumors were performed through open surgery, gaining access to the peritoneal cavity through a large abdominal incision (30 - 40 cm), including transection of the abdominal wall muscles. The presence of a large incision potentially underlies several post-operative complications, such as postoperative pain, wound infections and abdominal wall hernias (reported to be as high as 22% three years after laparotomy). [19] Cosmetically, patients are left with a large scar.

To mitigate the impact of the surgery on a patient and to reduce the aforementioned disadvantages of open surgery, conventional laparoscopy was developed several decades ago, aimed to perform surgical procedures in a minimally invasive manner. Patient benefits of a conventional laparoscopic surgical approach include less blood loss, fewer (major) complications and an enhanced recovery after surgery. [20-22] The first conventional laparoscopic organ resection was performed in 1975: a laparoscopic salpingectomy. [23] Since then, the technique has evolved; nowadays conventional laparoscopy is the gold standard approach in many procedures, such as appendectomy, cholecystectomy or colon resections. [24, 25] Over time, conventional laparoscopy was introduced in HPB surgery as well, although relatively late compared to the aforementioned procedures. The first laparoscopic liver and pancreatic resections were only reported in the early 90's. [26, 27]

This late introduction of conventional laparoscopic HPB surgery might be explained by the technical complex nature of liver and pancreatic resections. Moreover, severe complications are inherent to HPB surgery, thereby potentially restraining surgeons from performing these procedures through minimally invasive surgery. At present, studies reporting the feasibility of both laparoscopic liver and pancreatic resections have been published. [28-32] Widespread use of laparoscopic HPB surgery, however, is lagging behind, despite the fact that the technique was introduced almost three decades ago. There are several potential explanations for this. First, the technical impairments of conventional laparoscopy (most importantly: the non-articulating instruments, two-dimensional view, the fact that the surgeon is moving in opposite direction of what he/she sees on the screen and awkward ergonomics) might be too problematic for complex procedures such as in HPB surgery. [33] Second, since the technique is technically challenging, it is difficult and time-consuming to learn. Third, since not every procedure is suited for minimally invasive surgery, a hospital would need a large overall volume to select cases and still perform an adequate number of procedures. For example, Adam et al. described inferior outcomes if less than 22 minimally invasive pancreatoduodenectomies are performed annually. [34] Furthermore, several disadvantages of laparoscopic HPB surgery have emerged over these past decades, further explained hereafter.

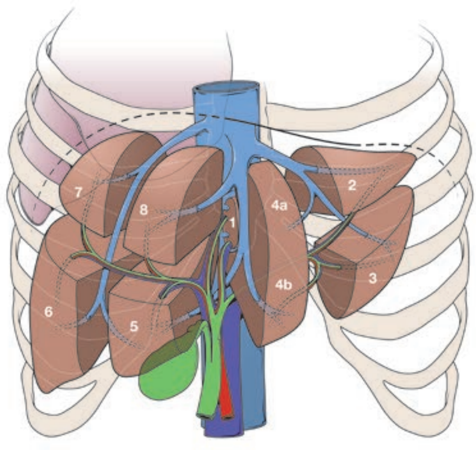

Figure 2. Schematic overview of Couinaud's classification of the liver segments. The posterosuperior segments (1, 4A, 7 and 8) are difficult to reach with rigid laparoscopic instruments due to their location.

Laparoscopic liver resection

For liver resection, acceptable outcomes of several thousand laparoscopic liver resections have been published, ranging from small wedge resections to (extended) hemihepatectomies. [28] The procedure is, however, described as technically demanding. In particular, resections of the posterosuperior segments (1, 4A, 7 and 8) are considered difficult. This may be explained by the fact that these segments are nearly impossible to reach with the non-wristed straight laparoscopic instruments. (Figure 2) In studies on conventional laparoscopic liver resection, resections of the posterosuperior segments were independently predictive for conversion to laparotomy and associated with longer operative times and increased blood loss, when compared to resections of the anterolateral segments (2, 3, 4B, 5 and 6). [35-37] This is also reflected in the Louisville Statement, the international consensus paper on laparoscopic liver resection, and in the subsequent Marioka paper: laparoscopic resections of the posterosuperior segments are considered 'major' liver surgery and should not be standard of care, in contrast to laparoscopic resections of the anterolateral segments. [38, 39] To enable laparoscopic resection of the posterosuperior segments, technical modifications were devised, such as the placement of a trans-thoracic trocar or hand-assistance. However, the hand-assistance technique has not solved the problem of restricted visualization and requires an extra (large transthoracic) incision. Furthermore, the trans-thoracic approach holds the risk of seeding of the malignancy to the chest and pleural effusion. Moreover a chest tube has to placed afterwards.[40, 41]

In summary, several aspects of liver resection require optimal dexterity and visualization, such as resections of the posterosuperior segments, hilar dissection or working in a curved transection plane. Although laparoscopy seems an adequate approach for some types of liver resection, the technical limitations of conventional laparoscopy make the technique insufficient for the entire spectrum of liver surgery.

Laparoscopic pancreatic resection

Laparoscopic pancreatic surgery has become a popular research topic in recent years, resulting in several (Dutch) randomized controlled trials comparing laparoscopic with open approaches, for both pancreatoduodenectomy and distal pancreatectomy. [42-44]

In the Dutch multicenter LEOPARD trial patients with left-sided pancreatic lesions were randomly assigned to either undergo minimally invasive distal pancreatectomy (eventually: 89% conventional laparoscopic, 11% robotic) or open distal pancreatectomy, aimed to compare time to functional recovery. [42] Results demonstrated a shorter time to functional recovery in the minimally invasive group (4 days (IQR: 3-6) versus 6 days (IQR: 5-8), $p < 0.001$). Other benefits of the minimally invasive approach included less delayed gastric emptying, improved quality of life and equal costs. In contrast, the laparoscopic approach took significantly longer and there was no reduction in the overall occurrence of postoperative complications.

Laparoscopy was expected to offer several short-term benefits in pancreatoduodenectomy as well. Two randomized controlled trials, one from India and one from Spain, compared laparoscopic with open pancreatoduodenectomy. [43, 44] Although the results of these trials were promising and demonstrated feasibility and safety of the technique, a subsequent Dutch randomized controlled trial (LEOPARD-2) comparing minimally invasive pancreatoduodenectomy with the open approach was terminated prematurely due to safety concerns of the laparoscopic technique and a (statistically non-significant) increase in complication-related 90-day mortality in the laparoscopic group (10% vs. 2%; $p = 0.2$). [45] As a consequence, a national consensus meeting concluded that pancreatoduodenectomy should no longer be performed using conventional laparoscopy in the Netherlands. Potential explanations given for the unexpected outcome of this trial included the limited volume in some of the participating centers and the long learning curve of the technique.

In summary, conventional laparoscopy appears to be a safe and feasible approach for distal pancreatectomy, with potential benefits for the patient. For pancreatoduodenectomy however, the technique does not seem suited. Possibly, the construction of the three anastomoses in pancreatoduodenectomy requires a higher level of surgical precision and dexterity than can be accomplished with conventional laparoscopy.

Robotic surgery and its potential in HPB surgery

To overcome the technical limitations of conventional laparoscopy and enabling minimally invasive surgery with the same dexterity as open surgery, the surgical robot was introduced. Robotic instrumentation is wristed with a wider range of motion than the human hand and the surgical field displayed in the console is magnified and three-dimensional. Moreover, the surgeon's movements are scaled, tremors are filtered and ergonomics are improved. [33] Robotic surgery does have some disadvantages, including increased costs. [46] However, costs are expected to decrease when new robotic systems will enter the market. [47] The second most often reported disadvantage concerns the lack of haptic feedback.

In 2000 the US Food and Drug Administration (FDA) approved the da Vinci surgical robot from Intuitive Surgical (Intuitive Surgical Inc., Sunnyvale, CA, USA) for the US market. The device was inspired by the call for telesurgical machines for President Dwight Eisenhower's Defense Advanced Research Projects Agency (DARPA). DARPA intended to develop remote surgery technology to treat wounded soldiers in war zones from a distance with telesurgery. Intuitive Surgical seized the opportunity for the civilian market, bought the patents, and subsequently developed the first generation of da Vinci surgical robots. The da Vinci surgical robot was initially approved for general surgery, but not long after its entrance on the market it found its way into minimally invasive surgery in many specialties. Over the past decades, indications have rapidly expanded. [48, 49] Recent studies on trends in the United States show a strong increase in the use of robotic surgery for a wide spectrum of surgical specialties, including general surgery, urology, gynaecology and cardiothoracic surgery. [50-52]

The surgical robot allows the surgeon to perform minimally invasive surgery with at least the same dexterity as in open surgery and with potentially better visualization (three-dimensional vision and strongly magnified). The use of the robot might be especially beneficial in procedures that require meticulous dissection, extensive suturing, or working in curved transection planes. This would render robotic assistance ideally suited for HPB surgery. In this thesis, we aimed to describe the set-up of a comprehensive program for robotic HPB surgery, notably robotic liver resection as well as robotic pancreatoduodenectomy in the Netherlands. We address the steps involved in safe initiation and implementation of such a program, delineate several aspects of the surgical technique and assess initial outcomes, all focused on the safe introduction of a new technique and aimed to improve outcomes of patients undergoing these major surgeries.

Thesis Outline

Robotic liver surgery

In **chapter 2** we have performed a systematic review to provide an overview of the indications, surgical details and outcomes of robotic liver resection. Introduction of a new surgical technique, such as robotic surgery in HPB surgery, is not (yet) subject to formal surveillance of a medical ethics committee or any other authority. However, several preconditions must be met prior to the start of a successful robotic program. The set-up of a robotic program for liver surgery is described in **chapter 3.** Initial results of the first robotic liver resections performed in the UMC Utrecht, including resections of the posterosuperior segments, are presented in **chapter 4**. **Chapter 5** describes a multi-institutional, multinational study from four expert centers worldwide (Memorial Sloan Kettering Cancer Center, City of Hope Comprehensive Cancer Center, Yonsei University Health System and University Medical Center Utrecht). In this chapter, robotic liver resections of the posterosuperior segments are compared after propensity score matching to open resections of these segments, hypothesizing that this group of resections might benefit in particular from robotic technology. **Chapter 6** describes the operative details and postoperative outcomes of 70 robotic liver resections during which the robotic Vessel Sealer (Extend) was used for parenchymal transection. A video of a robotic right hepatectomy for a central liver tumor is presented in **chapter 7.1,** demonstrating the technical advantages of robotic technology in complex procedures. In **chapter 7.2**, a video describing step-by-step robotic liver resection of segment 7 is provided.

Robotic pancreatic surgery

Part 2 of this thesis focuses on the implementation and initial results of robotic pancreatic surgery in the Netherlands. In **chapter 8** the initiation of robotic pancreatic surgery in the Netherlands and the set-up of a nationwide training program are presented. In **chapter 9** the stepwise implementation and expansion of robotic HPB surgery in a larger group of surgeons is described. **Chapter 10** again illustrates the benefits of robotic technology in a comprehensive video of a robotic pancreatoduodenectomy in a 10-year-old child with a solid pseudopapillary neoplasm. Overall results of the first 100 robotic pancreatoduodenectomies performed in the Netherlands in three centers (Regional

Academic Cancer Center Utrecht, Erasmus Medical Center and Maasstad Hospital) are presented in **chapter 11**. Lastly, in **chapter 12**, we compared short-term and long-term oncologic outcomes after robotic distal pancreatectomy to the outcomes of conventional laparoscopic distal pancreatectomy in a study from the American National Cancer Database.

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Part 1

Robotic Liver Surgery

Chapter 2

Robot-assisted Laparoscopic Liver Resection:

A Systematic Review and Pooled Analysis of Minor and Major Hepatectomies

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HPB (Oxford)
2016;18:113-120

Abstract

Background

Robotic surgery has been introduced to overcome the limitations of conventional laparoscopy. A systematic review and meta-analysis were performed to assess the safety and feasibility for three subgroups of robot-assisted laparoscopic liver resection: (1) minor resections of easily accessible segments: 2, 3, 4B, 5, 6, (2) minor resections of difficult located segments: 1, 4A, 7, 8 and (3) major resections: ≥ 4 segments.

Methods

A systematic search was performed in PubMed, EMBASE and Cochrane Library.

Results

Twelve observational, mostly retrospective studies reporting on 363 patients were included. Data were pooled and analyzed. For subgroup (1) (n = 81) the weighted mean operative time was 215 ± 65 min. One conversion (1%) to laparotomy was needed. Weighted mean operative time for subgroup (2) (n = 17) was 220 ± 60 min. No conversions were needed. For subgroup (3) (n = 99) the weighted mean operative time was 405 ± 100 min. In this subgroup 8 robotic procedures (8%) were converted to open surgery.

Conclusion

Data show that robot-assisted laparoscopic liver resection is feasible in minor resections of all segments and major resections. Larger, prospective studies are warranted to compare the possible advantages of robot-assisted surgery with conventional laparoscopy and open surgery.

Introduction

Liver resection was once considered a complex procedure, with high morbidity and mortality. Nowadays, liver resection is regarded a routine procedure. [1] Traditionally, liver resections are performed using laparotomy, but in the early 1990s minimally invasive techniques emerged. The first laparoscopic non-anatomic liver resection was performed in 1992 and the first anatomic liver resection in 1996.[2, 3] Since then, several non-randomized studies have shown that laparoscopic liver resection is safe and feasible in selected patients.[4, 5] Compared to open surgery, laparoscopic liver resection has been associated with less blood loss, shorter hospital stay and similar oncologic outcomes. [6-11] Laparoscopic liver resection was initially performed in patients with benign or peripherally located lesions. But, as time progressed, laparoscopic major hepatectomies and resections of the posterosuperior segments were also reported.[12-15]

However, laparoscopy has its disadvantages, most notably the limited mobility of the straight laparoscopic instruments. The robotic system provides a three-dimensional, magnified view of the operative field. This, in combination with the computer-to-human interface and wristed instruments, results in improved precision in surgical dissection. In theory, the improved dexterity makes robotic systems particularly suited for those resections that require non-linear manipulation, such as the curved parenchymal transection, hilar dissection and resection of the posterosuperior segments in liver surgery. Furthermore, the use of a robotic surgical system leads to decreased fatigue and tremor for the surgeon.[1, 16, 17]

Recently, a number of case series reporting on robotic liver resection have been published. It remains unclear from each of these series whether, in larger groups of patients, use of the robot is feasible and if the use of a robotic system is especially advantageous in a specific subgroup of liver resection. Hence, the aim of this review is twofold: First, to assess the feasibility and safety in terms of morbidity and mortality for all types of resections together; second, to perform a pooled analysis for three subgroups (minor resections of easily accessible segments, minor resections of difficult located segments, and major resections).

Methods

Study selection

A systematic search, restricted to papers published in English, up to 25-04-2015, was performed in PubMed, EMBASE and Cochrane Library. The study was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. [18]

Search terms were: '(robot OR robotic OR da Vinci) AND (liver OR hepatic OR hepatectomy OR liver resection OR hepatic resection)'. Titles and abstracts of the identified papers were screened. Two authors (CN and JH) examined full-text versions of papers considered for inclusion. The bibliographies of the selected articles were reviewed for other potentially relevant studies.

Eligibility criteria

Included were all clinical studies reporting on robotic liver resection, with full-text available in English. Studies focusing on biliary surgery, studies from which data were unavailable or insufficient, review articles and conference abstracts published in abstract form only, were excluded. Studies with sample size of fewer than five patients were also excluded. Disagreement on eligibility was addressed by discussion and consensus. Data were carefully examined to avoid double counting of patients and if multiple studies were published by one center, the study reporting the largest number of patients was selected for inclusion, unless it was clear data did not overlap.

Methodological quality

Two authors (CN and JH) assessed methodological quality of the included studies independently. Since all of the included studies were cohort studies, grading was performed using the Newcastle-Ottawa quality assessment scale (NOS).[19]

Data extraction

Data extracted from the selected studies included country, study design, study interval, relevant patients, total number of patients in the study, type of resection and whether comparisons were made between robotic, laparoscopic and open surgery. Patient demographics extracted from the selected studies included: sex, age, ASA score, previous abdominal surgery, number of lesions, tumor size and histopathology of the resected specimen. BMI is not presented in the tables, since only four of the included studies provided data on this and presentation was very heterogeneous. Documented data on (outcomes of) surgery included: operating time, blood loss, conversion rate, transection method, number of positive surgical margins, complication rate, length of hospital stay and mortality. Pooled data were analyzed for three different subgroups of resections: (1) minor resections of easily accessible segments: 2, 3, 4B, 5, 6. (2) Minor resections of difficult to reach segments: 1, 4A, 7, 8. (3) Major resections: ≥ 4 segments. [20, 21] If studies did not report outcomes separately for the different segments or resection types, authors were contacted to provide the additional data.

Statistical analyses

If studies documented the outcomes as medians and ranges, means and standard deviations (SD) were estimated according to the methods described by Hozo et al.[22] Weighted means and weighted SDs were calculated for all types of resection together and for the three separate subgroups of robot-assisted laparoscopic liver resection. Data regarding age, blood loss, operation time and tumor size are rounded in all tables. Data regarding length of stay are rounded to whole days.

Results

The search yielded a total of 799 studies. A total of 12 studies, one prospective [23] and eleven retrospective [24-34], including 363 relevant patients, met the inclusion criteria to be included in this systematic review. [23-45] (Figure 1) Study characteristics are summarized in Table 1. Four studies solely reported robotic procedures. Six studies compared outcomes for robot-assisted laparoscopic liver resection with conventional laparoscopic surgery. Two studies compared robot-assisted laparoscopic liver resection with conventional laparoscopic and open surgery.

Methodological quality

For all the included studies, details of the methodological quality are summarized in Table 2. Overall, the methodological quality of the included studies was adequate. However, almost all of the cohort studies included selected populations (e.g. excluding patients with vascular involvement, liver cirrhosis or tumor size >5 cm), which are not entirely representative for the general patient population undergoing liver resection. Most of the included studies were retrospective. [24-34] However, data from five studies were extracted from prospectively maintained databases. [24, 27-30]

Outcomes for all types of resection and pooled analysis

Patient characteristics and surgical outcomes of all resections are provided in Table 3 and Table 4. Pooled data for the different resection subgroups are summarized in Table 5. Outcomes by individual subgroup type are provided as supplementary material. (See Appendix: Supplementary Tables 1-3).

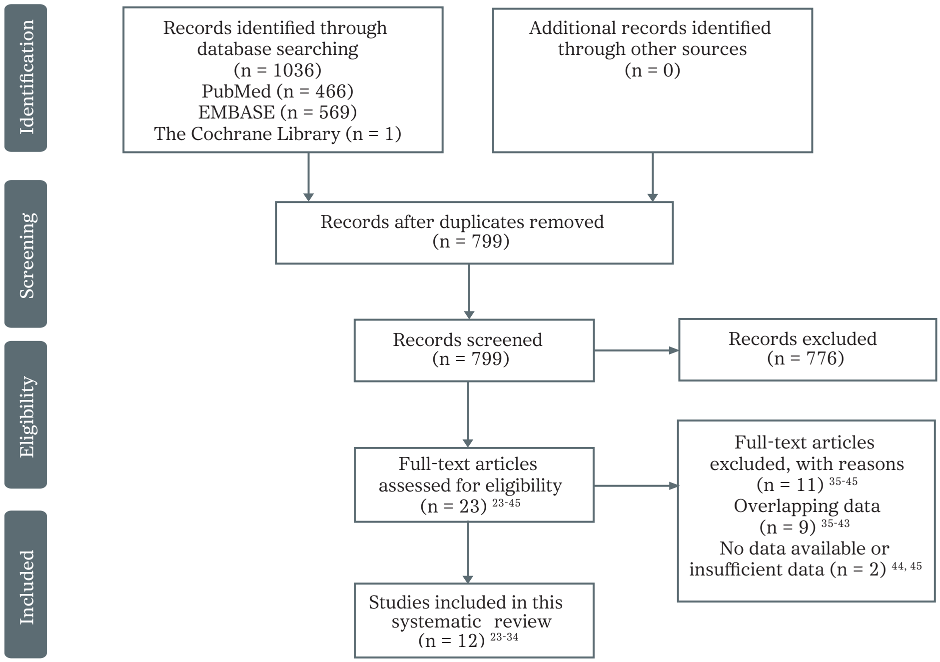

Figure 1. Flow diagram of the included studies

Table 1. Study characteristics

Authors	Country	Study interval	Relevant patients / total patients in study	Robotic procedures sorted per subgroup 1,2,3 (n)	
Giulianotti et al.	USA & Italy	Mar. 2002 - Mar. 2009	70/70	1/2	(43)
				3	(27)
Tsung et al.	USA	Nov. 2007- Dec. 2011	57/171	1	(31)
				2	(5)
				3	(21)
Wu et al.	Taiwan	2012	38/121	1/2	(39)
				3	(13)
Lai et al.	China	May 2009 - Mar. 2012	41/41	1/2	(33)
				3	(10)
Troisi et al.	Italy & Belgium	Mar. 2008 - Mar. 2012	40/263	1/2	(40)
				3	(0)
Choi et al.	Korea	Nov. 2008 - Apr. 2011	30/30	1	(8)
				2	(2)
				3	(20)
Spampinato et al.	Italy	Jan. 2009 - Dec. 2012	25/50	1	(0)
				2	(0)
				3	(25)
Felli et al.	Italy	Apr. 2013 - May 2014	20/20	1	(12)
				2	(6)
				3	(2)
Ji et al.	China	Apr. 2009 - Jul. 2009	13/65	1	(4)
				2	(0)
				3	(9)
Yu et al.	Korea	Jul. 2007 - Oct. 2011	13/30	1	(10)
				2	(0)
				3	(3)
Berber et al.	USA	Oct. 2008 - Sep. 2009	9/32	1/2	(9)
				3	(0)
Kandil et al.	USA	Feb. 2011 - Aug. 2011	7/7	1	(5)
				2	(1)
				3	(1)

Table 2. Assessment of methodological quality for cohort studies

	Selection				Comparability	Outcome		
Authors	Representiveness	Selection of controls	Ascertainment	Outcome of interest not present at start study	Comparability of cohorts	Assessment of outcome	Length follow-up	Adequacy of follow-up
Giulianotti et al.	❖	-	■	-	-	■	❖	■
Tsung et al.	■	■	■	-	■	■	■	■
Wu et al.	❖	■	■	-	❖	■	■	■
Lai et al.	❖	■	■	-	❖	■	■	■
Troisi et al.	❖	❑	■	-	❖	■	■	■
Choi et al.	❖	-	■	-	-	■	■	■
Spampinato et al.	❖	❑	■	-	❖	■	■	■
Felli et al.	❖	-	■	-	-	■	■	■
Ji et al.	❖	■	■	-	■	■	❖	■
Yu et al.	❑	■	■	-	❖	■	❖	■
Berber et al.	❖	■	■	-	❖	■	■	■
Kandil et al.	❖	-	■	-	-	■	❖	■

Legend: ■: consistent with criteria, low risk of bias; ❖: partially consistent with criteria, unknown risk of bias; ❑: not consistent with criteria, high risk of bias; -: not applicable.

Table 3. Patient characteristics

Authors	Male gender, n (%)	Age, years	ASA score, n (%)	Previous abdominal surgery, n (%)	Patients with cirrhosis, n (%)	Number of lesions, n	Tumor size, mm	Pathology, n (%)
Giulianotti et al.	30 (43)	60 (20-85)[c]	ASA 1: 13 (19) ASA 2: 29 (41) ASA 3: 28 (40)	34 (49)	8 (11)	1 (0-6)[b]	50 (10-110)[e]	malignant: 42 (60) benign: 28 (40)
Tsung et al.	24 (42)	60 ± 15[a]	ASA 1: 0 (0) ASA 2: 8 (14) ASA 3: 42 (74) ASA 4: 7 (12)	NR	3 (5)	1 (1-2)[b]	30 (20-50)[f]	malignant: 28 (49) benign: 19 (33) other: 10 (18)
Wu et al.	32 (84)	60 ± 15[a]	NR	NR	NR	NR	35 ± 15[a]	malignant: 38 (100)
Lai et al.	31 (75)	60 ± 10[a]	NR	NR	34 (83)	NR	35 ± 20[a]	malignant: 42 (100)
Troisi et al.	27 (68)	65 ± 10[a]	NR	13 (33)	NR	NR	NR	malignant: 28 (70) benign: 10 (25) other: 2 (5)
Choi et al.	14 (47)	50 (30-70)[c]	NR	NR	5 (17)	'single': 20 'multiple': 3	30 (10-50)[c,^]	malignant: 21 (70) benign: 9 (30)
Spampinato et al.	13 (52)	65 (30-80)[b]	ASA 1: 2 (8) ASA 2: 20 (80) ASA 3: 3 (12)	16 (64)	NR	NR	NR	malignant: 17 (68) benign: 8 (32)
Felli et al.	8 (40)	65 (50-80)[c]	ASA 1: 5 (25) ASA 2: 9 (45) ASA 3: 6 (30)	11 (55)	6 (30)	1*	35 (10-120)[c]	malignant: 17 (85) benign: 3 (15)
Ji et al.	9 (69)	55 (40-80)[c]	NR	2 (15)	4 (31)	NR	65 (20-120)[c]	malignant: 8 (62) benign: 5 (38)
Yu et al.	7 (54)	50 ± 10[a]	NR	NR	4 (31)	NR	30 ± 15[a]	malignant: 10 (77) benign: 3 (23)
Berber et al.	7 (78)	65 ± 5[d]	NR	NR	NR	NR	30 ± 15[d]	malignant: 7 (78) other: 2 (22)
Kandil et al.	5 (71)	45 (20-70)[c]	NR	NR	NR	NR	40 ± 35[a]	malignant: 4 (57) benign: 3 (43)

Abbreviations: ASA: American Society of Anesthesiologists; NR: not reported. Legend: [a] reported as mean ± SD; [b] reported as median (range); [c] reported as mean (range); [d] reported as mean ± SEM; [e] reported as weighted mean (range); [f] reported as median (IQR); * all lesions were solitary lesions; ^ only reported for hepatocellular carcinoma.

Table 4. Surgical outcomes all studies

Authors	Operating time, min.	Blood loss, mL	Conversion rate, n (%)	LoS, days	Positive surgical margins / malignancies	Transection method	Patients with ≥ 1 complication, n (%)	Mortality, n (%)
Giulianotti et al.	270 (90-660) [b]	260 (20-2000) [b]	4 (6)	7 (2-26)[b]	0/42	Harmonic device and bipolar forceps	15 (21)	0 (0)
Tsung et al.	255 (62-597) [b]	200 (30-3600) [b]	4 (7)	4 (1-31)[b]	2/42	NR	11 (19)	0 (0)
Wu et al.	380 ± 165[a]	325 ± 480[a]	2 (5)	8 ± 5[a]	NR	NR	3 (8)	0 (0)
Lai et al.	230 ± 85[a]	415 (10-3500)[b]	2 (5)	6 ± 4[a]	3/42	NR	3 (7)	0 (0)
Troisi et al.	270 ± 100[a]	330 ± 300[a]	8 (20)	6 ± 3[a]	3/28	Straight-line: Harmonic scalpel Curved and angulated section lines: Kelly Clamp crushing technique using EndoWrist Precise bipolar forceps	5 (13)	0 (0)
Choi et al.	510 (120-815)[c]	345 (95-1500)[c]	2 (7)	12 (5-46)[b]	0/13	Harmonic curved shears and Maryland bipolar forceps	13 (43)	0 (0)
Spampinato et al.	430 (240-725)[b]	250 (100-1900)[b]	1 (4)	8 (4-22)[b]	0/17	NR	4 (16)	0 (0)
Felli et al.	140 (100-200)[c]	50 (0-200)[c]	0 (0)	6 (4-14)[b]	2/17	Combination of Kelly Clamp crushing technique, bipolar forceps, monopolar crochet and Harmonic scalpel	2 (10)	0 (0)
Ji et al.	340 (150–720)[c]	280[e]	0 (0)	7[e]	0/8	Harmonic curved shears and bipolar electrocautery	1 (8)	NR
Yu et al.	290 ± 85[a]	390 ± 65[a]	0 (0)	8 ± 2[a]	0/10	Harmonic scalpel	0 (0)	0 (0)
Berber et al.	260 ± 30[d]	135 ± 60[d]	1 (11)	NR	0/9	Harmonic scalpel, clips, scissors or stapler	1 (11)	NR
Kandil et al.	60 ± 30[a]	100 (10-200)[c]	0 (0)	2 (1-5)[b]	NR	Harmonic scalpel	2 (29)	0 (0)

Abbreviations: NR: not reported; LoS: length of stay. Legend: [a] reported as mean ± SD; [b] reported as median (range); [c] reported as mean (range); [d] reported as mean ± SEM; [e] reported as mean.

Table 5. Pooled surgical outcomes

	Group	Patients, n	Operating time, min. *	Blood loss, mL *	Conversion rate, n (%)	LoS, days *	Positive surgical margins, n (%)	Patients with ≥ 1 complication, n (%)	Mortality, n (%)
	All types of resection	363	300 ± 130	300 ± 575	24 (7)	7 ± 6	10 (4)	60 (17)	0 (0)
1	Minor resections: 2, 3, 4B, 5, 6	81	215 ± 65	230 ± 310	1 (1)	5 ± 2	2 (2)	15 (19)	0 (0)
2	Minor resections: 1, 4A, 7, 8	17	220 ± 60	170 ± 120	0 (0)	5 ± 1	2 (12)	4 (24)	0 (0)
3	Resections of 4 or more segments	99	405 ± 100	380± 505	8 (8)	11 ± 6	0 (0)	26 (26)	0 (0)

Abbreviations: LoS: length of stay. Legend: * reported as mean ± SD.

Discussion

Here, the largest review on robot-assisted laparoscopic liver resections to date as well as the first pooled analysis for subgroups of liver resection are provided. Collectively, the data show that the robotic platform is safe and suitable in all subgroups of liver resection in terms of operative time, blood loss, and number of conversions. Evidently, the fact that all published series so far selected patients must be taken into account. Larger, prospective series are therefore needed to confirm the suitability of robot-assisted laparoscopic surgery.

It remains to be determined if the robotic platform provides definitive advantages over standard laparoscopy in liver surgery. The data show significantly longer operating times for robot-assisted liver resection over conventional laparoscopic liver resection. However, this finding is biased by the fact that the learning curve of robot-assisted laparoscopic liver resection had not been completed, as most series included here represent initial experience. As was shown by Tsung et al., operating time, as well as blood loss and length of stay, significantly decrease as experience grows. [31] Moreover, it will be interesting to learn if robot-assisted laparoscopic liver resection has steeper learning curves than conventional laparoscopy, as was shown previously in complex minimally invasive abdominal surgery such as pancreatic resection. [46] The data show that conversion rates are low in any subgroup (1%, 0%, and 8% respectively in groups 1, 2, and 3). Although group 2 included 17 patients only, the data suggest that the robotic platform may be of particular advantage in resections of the posterosuperior segments. [1, 47] In comparison, studies reporting on minor laparoscopic resections of the posterosuperior segments describe the technique as technically challenging. Moreover, when comparing converted procedures versus non-converted procedures, there are significantly more posterosuperior segments resections in the converted group (12.7% vs. 2.5%). [47, 48] This is in line with the 2008 Louisville statement, which recommends laparoscopic liver resection for lesions located in segments 2 to 6, but recommended that laparoscopic resections of segments 1, 7 and 8 should not be considered as standard of care due to their difficult to reach location. [20] In major liver resection, use of the robotic platform leads to a larger number of procedures performed totally laparoscopically. [31]

Taken together, the data show that robot-assisted laparoscopic liver resection is suitable for both minor and major resections. The authors speculate that minimally invasive approaches to liver surgery, nowadays still widely performed in an open manner, will more likely come through robotic surgery. Since in minor liver resection, rather than in major resection, size of the incision dominates postoperative recovery, it is suggested that the greatest potential clinical benefit of the robotic platform lies in minor resection of difficult located lesions.

How to proceed with further clinical implementation?

First, surgical technique needs to be refined and clarified in larger studies. For instance, it remains unclear which technique is best for parenchymal transection during robotic liver resection. Wristed (bipolar forceps, PK dissector, Vessel Sealer) as well as non-wristed (Harmonic curved shears) coagulation devices, as well as clip appliers, staplers, and plain sutures may all be suitable for precise parenchymal dissection, however, their comparison needs to be worked out. As of yet, the CUSA system, widely used in open and laparoscopic liver surgery, is not available for the robotic platform. Also, optimal patient position, port placement, and possible elimination of transthoracic trocars in segment 7-8 resections needs to be clarified along with novel applications such as indocyanine-green biliary contrast (FireFly imaging) and integrated augmented-reality navigation. Second, cost of the robot-assisted laparoscopic liver resection compared to conventional laparoscopy needs to be assessed.

Conclusion

In conclusion, based on the currently available literature, robot-assisted liver resection seems to be safe and feasible in selected patients for all categories of liver resection. The real benefit of the use of a robotic system over conventional laparoscopy presumably lies in minor resections of the posterior segments. However, given the limited number of available studies, large randomized studies are needed to compare robot-assisted surgery with conventional laparoscopy and open surgery.

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Appendix - Supplementary Material Chapter 2

Supplementary Table 1. Surgical outcomes of minor resections of segments 2, 3, 4B, 5, 6

Authors	Patients, n	Operating time, min.*	Blood loss, mL*	Conversion rate, n (%)	LoS, days*	Positive surgical margins ,n (%)	Patients with ≥ 1 complication, n (%)	Mortality, n (%)
Giulianotti et al.	17	(4 pt.) 4B&5: 265 ± 70 (4 pt.) 5&6: 170 ± 40 (9 pt.) 2&3: 215 ± 70	(4 pt.) 4B&5: 225 ± 60 (4 pt.) 5&6: 215 ± 60 (9 pt.) 2&3: 530 ± 560	1 (6)	(4 pt.) 4B&5: 7 ± 2 (4 pt.) 5&6: 5± 2 (9 pt.) 2&3: 7 ± 4	0 (0)	3 (18)	0 (0)
Tsung et al.	29	210 ± 70	240 ± 390	0 (0)	4 ± 2	1 (3)	5 (17)	0 (0)
Choi et al.	8	(4 pt.) 2&3: 450 ± 100 (2 pt.) 4B&5: 535 ± 160 (2 pt.) 6: 200 ± 110	(4 pt.) 2&3: 215 ± 50 (2 pt.) 4B&5: 140 ± 55 (2 pt.) 6: 150 ±75	0 (0)	(4 pt.) 2&3: 8 ± 1 (2 pt.) 4B&5: 7 ± NR (2 pt.) 6: 10 ± 3	0 (0)	5 (63)	0 (0)
Felli et al.	12	140 ± 25	60 ± 60	0 (0)	5 ± 2	1 (8)	0 (0)	0 (0)
Yu et al.	10	255 ± 50	275 ± 100	0 (0)	8 ± 2	0 (0)	0 (0)	0 (0)
Kandil et al.	5	50 ± 25	60 ± 80	0 (0)	2 ± 2	NR	2 (40)	0 (0)

Abbreviations: NR: not reported; pt.: patients; LoS: length of stay. Legend: * reported as mean ± SD.

Supplementary Table 2. Surgical outcomes of minor resections of segments 1, 4A, 7, 8

Authors	Patients, n	Operating time, min. *	Blood loss, mL *	Conversion rate, n (%)	LoS, days *	Positive surgical margins, n (%)	Patients with ≥ 1 complication, n (%)	Mortality, n (%)
Giulianotti et al.	3	240 ± 85	360 ± 260	0 (0)	7 ± NR	0 (0)	1 (33)	0 (0)
Tsung et al.	5	310 ± 55	175 ± 80	0 (0)	4 ± 1	1 (20)	1 (20)	0 (0)
Choi et al.	2	255 ± 105	250 ± 70	0 (0)	8 ± 4	0 (0)	1 (50)	0 (0)
Felli et al.	6	145 ± 20	30 ± 15	0 (0)	5 ± 1	1 (17)	1 (17)	0 (0)
Kandil et al.	1	85	200	0 (0)	2	NR	0 (0)	0 (0)

Abbreviations: NR: not reported; LoS: length of stay. Legend: * reported as mean ± SD.

Supplementary Table 3. Surgical outcomes of resections of ≥ 4 segments

Authors	Patients, n	Operating time, min. *	Blood loss, mL *	Conversion rate, n (%)	LoS, days *	Positive surgical margins, n (%)	Patients with ≥ 1 complication, n (%)	Mortality, n (%)
Giulianotti et al.	27	315 ± 65	300 ± 475	1 (4)	Italy: 10 ± 5 US: 6 ± 1	0 (0)	8 (30)	0 (0)
Tsung et al.	21	355 ± 120	430 ± 765	4 (19)	7 ± 6	0 (0)	5 (24)	0 (0)
Choi et al.	20	(14 pt.) left: 520 ± 130 (6 pt.) right: 725 ± 50	(14 pt.) left: 330 ± 245 (6 pt.) right: 630 ± 415	2 (10)	(14 pt.) left: 16 ± 8 (6 pt.) right: 23 ± 11	0 (0)	8 (40)	0 (0)
Spampinato et al.	25	435 ± 110	420 ± 405	1 (4)	9 ± 4	0 (0)	4 (16)	0 (0)
Yu et al.	3	410 ± 10	350 ± 70	0 (0)	8 ± 1	0 (0)	0 (0)	0 (0)
Felli et al.	2	165 ± 20	55 ± 25	0 (0)	9 ± 3	0 (0)	1 (50)	0 (0)
Kandil et al.	1	90	200	0 (0)	2	NR	0 (0)	0 (0)

Abbreviations: NR: not reported; LoS: length of stay. Legend: * reported as mean ± SD.

Chapter 3

Setting Up a Robotic Hepatectomy Program:

A Western-European Experience And Perspective

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Abstract

Currently the majority of liver resections are performed via open resection. Nevertheless, minimally invasive liver surgery is gaining ground and conventional laparoscopy has proven to be beneficial in different fields of liver surgery compared to open resections. Still, conventional laparoscopy has a few downsides, from which straight instruments, two-dimensional view and awkward ergonomics are the most obvious. The robotic surgical system is developed to overcome these limitations. It offers several advantages over conventional laparoscopy to optimize conditions in minimally invasive surgery: instruments are wristed with a wide range of motion and the view is three-dimensional and magnified. With instruments with a greater range of motion than in laparoscopic surgery, the use of a robotic system potentially broadens indications for minimally invasive liver resection. Here, we discuss the steps of setting up a robotic hepatectomy program against the background of the initial experience at our institution.

Introduction

An increasing proportion of gastrointestinal procedures are performed through minimally invasive surgery. Nowadays, even complex procedures such as pancreatic and liver resections are done in a minimally invasive way. [1-3] While in both pancreatic and liver surgery randomized clinical trials on patient benefit are underway, extensive non-randomized studies have already compared open with laparoscopic liver resection. Compared to open surgery, the laparoscopic approach has been associated with similar oncologic outcomes, shorter hospital stay and less blood loss, most evidently in minor liver resections. [4-8]

Consequently, since the first conventional laparoscopic liver resection in 1992 [9], this technique has been gradually adopted by more and more predominantly very large hospitals. Surprisingly, however, the percentage of liver resections performed laparoscopically on a national health care level in many countries lags far behind that of other gastrointestinal (e.g. colorectal) procedures. For instance, in the Netherlands in 2014 only 11% of liver resections were performed laparoscopically. [10] Slow adoption of minimally invasive liver surgery may be due to the more complex anatomy of the liver, a highly vascularized solid organ, and the fact that many dedicated hepatobiliary and HPB surgeons are still “open” surgeons. The disadvantages of conventional laparoscopy (such as straight instruments with a 1-dimensional working axis and troublesome optics) are, therefore, most pronounced in liver surgery.

The use of a robotic surgical system can resolve these downsides of conventional laparoscopy. The view of the robotic system is three-dimensional and instruments are wristed, with a range of motion greater than the human wrist. Robotic instrumentation may thus facilitate, for instance, curved parenchymal transection lines or dissection at the liver hilum. An additional advantage is less surgeon fatigue, especially in longer procedures. [11, 12] More than 400 robotic liver resections have recently been described in the literature [13, reviewed in 14], showing that robotic liver resection is safe and feasible, and may especially be of clinical advantage in smaller, ill-located partial hepatectomies.

In this review, we present our initial robotic hepatectomy case series and discuss the steps of setting up a robotic hepatectomy program against the background of the University Medical Center (UMC) Utrecht experience.

Initial experience with robotic hepatectomy at UMC Utrecht

Since the start of the robotic hepatectomy program in August 2014, the hepato-pancreato-biliary (HPB) team at UMC Utrecht performed 24 robotic liver surgeries.

In summary, five patients underwent a total of six cyst fenestration procedures [in part published, 15] and eighteen patients underwent a partial hepatectomy. (Tables 1-3) All procedures were fully laparoscopic-robotic. Fourteen patients had had previous abdominal surgery, including three who had undergone liver surgery before. In the partial hepatectomies, a total of 21 resections were performed in seventeen patients and one procedure was converted. The majority of the resections were performed for colorectal liver metastases. The median operative time for our robotic hepatectomies was 137 minutes. Four patients had a grade III complication and one patient had a grade IV complication (Clavien-Dindo). The patient who had a grade IV complication suffered from a pulmonary embolism postoperatively and was admitted to a medium care unit for two days. [16] We observed no grade V complications in our patients. In two of the patients with malignant disease, the surgical margin was positive (defined as tumor cells <1 mm distance to resection surface). Median length of hospital stay was 4 (range: 1-8) days. All patients visited our outpatient clinic after discharge: all had fully recovered and there were no wound healing problems.

Table 1. Robotic liver surgery in UMC Utrecht

Characteristic	n = ^
Procedures performed	24
Cyst fenestrations	6 procedures in 5 patients
Partial hepatectomies	18
Operative time cyst fenestrations, median (range), min.	108 (90-117)
Operative time partial hepatectomies, median (range), min.*	137 (60-265)
Patients who had previous abdominal surgery	14
Previous liver surgery	3
Conversion to laparotomy	1
Histopathology in partial hepatectomies	
Benign	2
Colorectal liver metastasis	12
Neuroendocrine tumor liver metastasis	1
Hepatocellular carcinoma	2
Cholangiocarcinoma	1
Patients with a postoperative complication*	8
≥ Clavien-Dindo grade III	5
Length of stay, median (range), days	4 (1-8)

Legend: * converted procedure excluded; ^ reported as ‘n’, unless stated otherwise.

Table 2. Segments resected in the robotic partial hepatectomies

Characteristic	n =
Procedures performed	18
Resections performed*	21
Wedge or segment	16 : 5
Segment 2	3
Segment 2/3	2
Segment 3	1
Segment 4B/5, wedge + gallbladder	2
Segment 5	2
Segment 6	1
Segment 7	7
Segment 8	3

Legend: * converted procedure excluded.

Table 3. Segments resected in the robotic cyst fenestrations

Characteristic	n =
Procedures performed	6
Polycystic liver disease	3
Segment 1	1
Segment 4B	1
Segment 7	1

Prerequisites for a robotic hepatectomy program

Several conditions must be met prior to starting the program. First and foremost, as anywhere in surgery, a successful program is a team effort. The team comprises the surgeons, as well as anesthesiology, OR staff, and robotic support staff. At the UMC Utrecht, we started out with two of the three HPB surgeons performing each procedure, with one surgeon at the console for the first ten procedures and the other surgeon at the tableside, and switch for the next ten. In this way, experience is built by the team while the learning curve is steep enough for the individual.

Second, equipment and available expertise are needed. The UMC Utrecht has one da Vinci robotic system (currently, the Si) in operation since 2000 that has mainly been used in urology and gastrointestinal oncology surgery. Thus, at the time of starting the hepatectomy program, there was wide experience available within our department with robotic esophagectomies, thyroidectomies, and distal pancreatectomies. While the HPB surgeons already had some experience performing robotic distal pancreatectomies (about 20 procedures performed by two surgeons), additional support was available from our upper-GI team and robotic physician assistant. In addition, the HPB surgeons all had extensive previous exposure in general surgical laparoscopy as well as limited experience with laparoscopic liver resection (mainly left lateral resections; around ten procedures performed per surgeon).

Third, proctoring is considered a crucial step in starting a program. Expertise worldwide in robotic liver resection, however, is sparse and still concentrated in a few hospitals. Therefore, in addition to official da Vinci console training (Paris, France), our team spent two multiple-day visits on case observations with prof. dr. Yuman Fong (Memorial Sloan Kettering Cancer Center, New York, NY, United States; currently: City of Hope Comprehensive Cancer Center, Duarte, CA, United States).

Patient selection

Patient characteristics

Indications for liver resection were set in our multidisciplinary HPB tumor board meeting. Individual patients were next selected for robotic hepatectomy by the staff HPB surgeons based mainly on lesion location (i.e. lesions suitable for wedge, one- or two-segment resection without need for dissection at the hilum). Certain specific patient characteristics were specifically taken into account. First, body mass index (BMI). BMI of patients in our series BMI ranged from 18-33 kg/m^2. Currently, there is no consensus on 'ideal' BMI for robotic liver surgery. Though, in extreme obesity or in patients with a very low BMI, it can be difficult to obtain enough working space and have adequate exposure. Furthermore, we excluded patients who had had very extensive abdominal surgery (e.g. complicated gastrointestinal procedures) and severe comorbidities, such as patients with abnormal coagulation or conditions that precluded the patient from lying in anti-Trendelenburg. Patients who had undergone liver surgery were not excluded, provided previous resection was in the contralateral hemiliver. In our initial series, we performed two redo robotic liver resections for colorectal metastases: a segment 2/3 metastasectomy after previous right trisectionectomy and a segment 2 metastasectomy after previous right hepatectomy.

Resection type

In the 2008 Louisville Statement, and in the 2014 meeting in Morioka, Japan, it is recommended that surgeons implementing a laparoscopic liver resection program start with minor resections (defined as two or less segments) of segment 2, 3, 4B, 5 and 6. In the statement, resections of the posterosuperior segments (1, 7, 8, 4A) are considered 'major resections' and were not accepted as standard of care. [17, 18]

We started our robotic hepatectomy program according to these recommendations and first performed resections of the anterior and inferior segments.

Alongside, robotic skill was further built with liver cyst fenestrations [15] and robotic distal pancreatectomies. However, due to the aforementioned benefits of the robotic system and based on first experience, we expected resections of the posterosuperior section to be technically less challenging robotically than with conventional laparoscopy. Hence, we successfully started early in the program with resections of segment 7 or 8.

Type of lesion

We performed the majority (12 out of 18 patients) of our resections for colorectal liver metastases (median lesion size 19 mm, range 9-57 mm), since these lesions are common in our practice and often easy to locate by ultrasound, or by vision when subcapsular.

Other resected lesions included adenoma, neuroendocrine liver metastasis, intrahepatic cholangiocarcinoma, and hepatocellular carcinoma (HCC). One of the two procedures we performed for a HCC was converted. This concerned a large (31 mm) HCC in segment 5 without clinical or radiological signs of liver cirrhosis or other parenchymal disease, which was deemed suitable for a wedge resection of segment 4B-5 along with the gallbladder. However, during surgery, the liver parenchyma appeared fibrotic and the lesion could not be properly delineated making it unclear if a safe oncologic margin could be obtained. The procedure was converted to a laparotomy, which resulted in a resection with a tumor free surgical margin. A cirrhotic or fibrotic liver can cause difficulties in parenchymal transection. Hence, although successful robotic resection for HCC has been reported in series from Asia [19], in our opinion, it would be preferable to not include HCCs in an initial hepatectomy program, or to beware of a low threshold for conversion.

Surgical technique and robotic instruments

Patient positioning

In resections of left-sided and anterior segments, patients are placed in a 15 to 30-degrees anti-Trendelenburg, French position. Four trocars are placed: one for the camera below the umbilicus, two robotic arms and a laparoscopic port for assistance. The robot is then docked over the patient’s head and the tableside assistant is positioned between the patient’s legs. For resections of

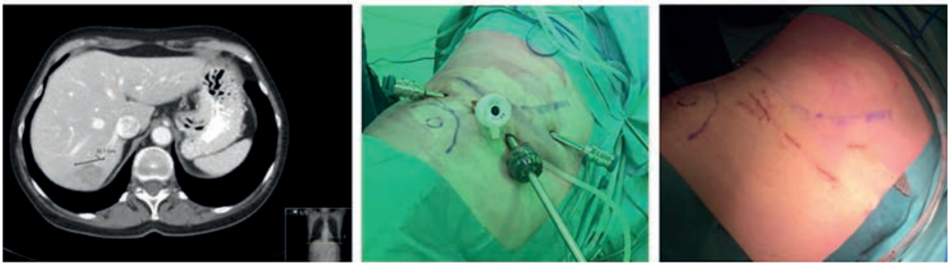

Figure 1. CT-scan, port placement and closed incisions of a patient who underwent a resection of a posterior segment

posterior segments, patients are placed in the left-lateral position. (Figure 1) Four trocars are placed, and a fifth trocar for assistance where appropriate. The robot is docked over the patient's head. All procedures were performed fully laparoscopic, no transthoracic trocars or hand ports were needed in any case.

Ultrasound and parenchymal transection

Intraoperative ultrasound is crucial in delineating oncological liver transection planes. We used a curved array 4-way laparoscopic transducer in our initial series (Hitachi Aloka Medical Inc., Wallingford, CT, USA). This laparoscopic transducer provided excellent imaging of the anterior liver segments, while imaging of segment 7 and segment 8 was felt to be less easy although adequate. Notably, a robotically controlled "drop-in" ultrasound transducer is on the market (Hitachi Aloka Medical Inc.) that may be of particular use in robotic liver surgery. [13]

There are several techniques for parenchymal transection in robotic liver surgery, presented in Table 4. It remains unclear, for both laparoscopic and robotic hepatectomy, which technique is best. In line with the absence of a clearly superior transection technique even in open surgery, it was recommended that surgeons should use the technique they are familiar with and that an individual assessment should be made per resection. [18, 20]

In open liver resection, the CUSA system is most frequently used in our center. This device is as of yet unavailable for the da Vinci Si surgical system. We mostly used a combination of the wristed Maryland bipolar and Vessel Sealer devices for parenchymal transection. The Endo GIA was used to control pedicles or larger branches of hepatic veins where deemed appropriate. A Pringle manoeuvre was applied in two patients.

TachoSil (Takeda Nederland b.v., Takeda, Zurich, Switzerland) was used on the resection surface where deemed appropriate. Given our initial experience with these novel transection techniques, a surgical drain was placed with low threshold (9 out of 24 patients). There were no postoperative bile leaks or hematomas in our initial patient series.

Combined procedures

In three patients we performed multiple segmentectomies in one procedure. In addition, two patients received a laparoscopic right hemicolectomy and sigmoidectomy, respectively, in the same procedure as their robotic hepatectomy. Standard laparoscopic colon resection was chosen in these cases, as a robotic hemicolectomy program is not set up in our hospital yet. Combining these procedures seems safe and feasible. This is in line with the largest case series on robotic hepatectomy to date, where 23 of the 70 patients underwent an associated surgical procedure.[21] For the laparoscopic colectomies, the robot was undocked and the patient repositioned and redraped. For one of the multi-segmentectomies, we performed right posterior resection first and then repositioned and redocked the robot to perform left sided resection. Potentially, the da Vinci Xi may overcome the inefficiency of redocking in such cases as it permits multi-quadrant surgery.

Anesthesia & perioperative care

All patients were operated under general anesthesia with the first ten patients receiving an epidural catheter for analgesia. However, we omitted epidural anesthesia after our 10th successful robotic hepatectomy and switched to patient-controlled analgesia where appropriate. Central venous pressure measurement, nasogastric tube placement and avoidance of excessive fluid administration were standard peroperative procedures per our liver resection protocol.

Postoperative care was according to the UMC Utrecht enhanced recovery after surgery (ERAS) protocol. Literature on ERAS specific for robotic hepatectomy

Table 4. Techniques for parenchymal transection in robotic hepatectomy

Transection method	Open/lap./robot	Best suited for	Pro	Con
Maryland bipolar forceps	R	Superficial coagulation, structural preparation	Wristed, subtle dissection	Inefficient for larger plane of transection
PK dissecting forceps	R	Subtle parenchymal dissection	Wristed, subtle dissection	Inefficient for larger plane of transection
Vessel Sealer	R	Parenchymal transection, vessel transection	Wristed, efficient and reliable parenchymal transection	Bulky head, more expensive (disposable)
Harmonic ACE	R, L	Parenchymal dissection	Efficient parenchymal transection	Non-wristed, risk of inadvertent tissue damage by 'hot leg'
EndoClips	R, L	Ligation of vessels	Reliable vessel sealing	Inefficient, size may not match vessel
CUSA system	O, L	Parenchymal dissection	Subtle and efficient parenchymal transection	Non-robotic (bedside assistant)
Stapling device	O, L	Ligation of larger vessels, parenchymal transection	Reliable sealing of large vessels	Less easy to manipulate; expensive for parenchymal transection

Abbreviations: R: robotic; L: laparoscopic; O: open.

is lacking. However, studies comparing ERAS versus traditional care for laparoscopic hepatectomy show that ERAS is safe and feasible and associated with less postoperative complications and a shorter hospital stay. Therefore, we used this protocol for our patients who underwent robotic hepatectomy. [22]

Evaluation and expansion of the program

The learning curve

Conventional laparoscopic liver resection may have a learning curve of up to 60 resections. [23] For minor laparoscopic liver resections alone, learning curves have been reported ranging from 22 to 35 resections. Major laparoscopic have longer reported learning curves: 45 to 60 cases.[24-26] Data on learning curves in robotic hepatectomy are not available. In would be interesting in the future to see if robotic hepatectomy has a steeper learning curve than laparoscopic hepatectomy. As for pancreatic resection for example: in pancreatic resection, regarded a highly complex procedure, a comparison has been made between learning curves in conventional laparoscopic resections and robotic resections. A significant shorter learning curve was shown for the robotic resections. [27]

Evaluation and expansion

Our initial experience with robotic hepatectomy shows that this technique is easily adopted, allows for even fully laparoscopic, parenchymal-sparing resections of ill-located liver lesions, and is associated with low morbidity and fast recovery. The further expansion of our program will include training of an additional HPB surgeon, volume expansion for the minor resections, dissemination of the technique in several other Dutch tertiary care hospitals to enable outcomes research, and emulation of the program with right and left hepatectomies in the near future.

Cost & healthcare context

As anywhere else, the use of robotics in surgery is under scrutiny. Downsides of the use of the robotic system frequently mentioned by media and health care providers focusing on pure laparoscopic surgery, are the presumed higher costs and the lack of evidence. Longer operative times and expensive equipment are two of the major reasons robotic surgery is expensive currently. Still, the potential shorter hospital stay and the fact that, theoretically, a larger proportion of liver resections can be performed minimally invasive, may compensate for this alongside the reduction in cost that may come from the introduction of competing robotic platforms in the near future. A recent study, comparing robotic with open liver resection, showed no difference in costs between these two techniques. [28] Moreover, robotic sealing devices like the Vessel Sealer may be relatively less expensive than multiple laparoscopic stapler loads. (Table 4)

Health insurance in the Netherlands is mandatory and comprises a “hybrid” healthcare system where insurance companies are private (most not-for-profit branches of larger comprehensive, for-profit insurers), while overall health care expenditure and pricing is under strong government control. Within this context, there is no additional reimbursement (yet) for robotic gastrointestinal surgical procedures. The university hospitals, however, have responsibility and funding for tertiary care as well as research and innovation. The robotic program of UMC Utrecht is, therefore, partially funded via these academic resources.

Conclusion

In conclusion, robotic liver surgery can be safely and relatively easy implemented, provided that the start of the program is well coordinated. Due to the earlier mentioned benefits, indications for robotic liver resections can potentially be expanded using a robotic surgical system. In our opinion, the widespread introduction of minimally invasive surgery in liver resection will be most likely through robotic surgery.

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Chapter 4

Robotic Liver Resection Including the Posterosuperior Segments:

Initial Experience

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Abstract

Background

Robot-assisted laparoscopy has been introduced to overcome the limitations of conventional laparoscopy. This technique has potential advantages over laparoscopy, such as increased dexterity, three-dimensional view, and a magnified view of the operative field. Therefore, improved dexterity may make a robotic system particularly suited for liver resections, which require non-linear manipulation, such as curved parenchymal transection, hilar dissection, and resection of posterosuperior segments.

Methods

Between August 2014 and March 2016, sixteen patients underwent robot-assisted laparoscopic liver resection at the University Medical Center Utrecht.

Results

Fifteen robot-assisted laparoscopic liver resections were performed in a minimally invasive manner. One procedure was converted. In eight patients, we performed a resection of a posterosuperior segment (segment 7 or 8). Median operating time was 146 min. (range: 60-265), and median blood loss was 150 mL (range: 5-600). Four patients had a Clavien-Dindo grade III complication. Median length of stay was 4 days (range: 1-8). There was no mortality.

Conclusion

This prospective study reporting on our initial experience with robot-assisted laparoscopic liver resection demonstrates that this technique is easily adopted, safe, and feasible for minor hepatectomies in selected patients. Moreover, it shows that the robotic platform also enables fully laparoscopic resections of the posterosuperior segments.

Introduction

Minimally invasive liver surgery has a relatively brief history. Compared to other gastrointestinal procedures, laparoscopy in liver surgery lags behind. In 1992, the first non-anatomic laparoscopic liver resection was performed, and the first anatomic laparoscopic liver resection was performed in 1996. [1, 2] Nowadays, minimally invasive techniques are widely accepted. Over 3000 laparoscopic liver resections have been reported in the literature, ranging from resections for malignant and benign lesions to donor procedures. [3, 4] Non-randomized studies have shown that laparoscopic liver resection is safe and feasible in selected patients. Moreover, when comparing the laparoscopic liver resection with open liver resection, the laparoscopic approach is associated with significantly shorter hospital stay, less blood loss, and similar oncologic outcomes. [5-9]

In the last few years, a new minimally invasive technique for liver resection emerged: robot-assisted laparoscopic liver resection. The robotic system has been designed to overcome the shortcomings of conventional laparoscopy. It provides increased dexterity, a three-dimensional, magnified view of the operative field and it leads to decreased fatigue for the surgeon. Presumed higher costs and the lack of randomized evidence for the use of robotics have been cited as potential downsides. [10] Anyway, robot-assisted laparoscopy is nowadays widely used in gastrointestinal, urological and gynaecological surgeries. However, in liver surgery, it is not extensively used. Currently, approximately 400 procedures have been described in the literature. [11]

The aforementioned advantages of the use of a robotic system lead to increased precision in surgical dissection. Theoretically, the use of a robotic system would especially be advantageous in resections that require non-linear manipulation such as resections of the posterosuperior segments and in hilar dissection and curved parenchymal transection. [12-14]

In this study, we describe our first experiences with minor liver resections using the da Vinci Si robotic system (Intuitive Surgical, Sunnyvale, CA). Sixteen consecutive, selected patients underwent robot-assisted laparoscopic minor liver resections. Among these were eight patients who underwent a resection of a posterosuperior segment.

Methods

The University Medical Center Utrecht has experience on robotic surgery for several years. Since 2000, robot-assisted esophagectomies are performed. In addition, also pancreatic resections and thyroidectomies are performed robotically. This experience was used to help in setting up the program for the robot-assisted laparoscopic liver resections.

Following this, the first sixteen patients underwent robot-assisted laparoscopic liver resection at the University Medical Center Utrecht using the da Vinci Si Surgical System (Intuitive Surgical) from August 2014 to March 2016.

Indications for hepatectomy were made in a multidisciplinary team meeting. Whether the patient underwent a robot-assisted laparoscopic hepatectomy or an open hepatectomy was based on lesion location and evaluation of overall clinical status.

Data regarding patient demographics, perioperative parameters, and post-operative outcomes were collected in a prospectively maintained database. Patient demographics included age, sex, body mass index (BMI), previous abdominal surgery, and preoperative chemotherapy status. Data on pathologic findings included histopathology, benign or malignant status, tumor size, and resection margin. Data on the (outcomes of) surgery included operating room (OR) time, operating time, docking time, console time, blood loss, transection method, R0/R1/R2 status, conversion rate, postoperative complications, length of hospital stay, and mortality.

Operating time was defined as the time from first incision to wound closure. Postoperative complications were defined and graded according to the Clavien-Dindo classification scale. [15] Complications were registered up to 90 days after surgery. Resection margins were considered negative when no tumor cells were present in the transection surface or within 1 mm of it (R0). Resection margins were considered positive when tumor cells were present in the transection surface of within 1 mm of it (R1) or if the tumor was not resected radical macroscopically (R2). Postoperative death was defined as death within 90 days after surgery.

In medians of surgical parameters and surgical outcomes, no data of the converted procedure were used. Data of this patient and procedure were only used in the calculation of age, BMI, docking time, previous abdominal surgery, and the percentage of the patients who were male. When calculating the overall OR time, patients who underwent an additional procedure were excluded.

Surgical technique

Room set-up and port placement for resections of anterior segments (2, 3, 4B, 5, and 6)

Patients who underwent a resection of an anterior segment were placed in a supine position, 30° anti-Trendelenburg. First, a 12 mm trocar was placed in the umbilicus for camera introduction. Pneumoperitoneum was established to 15 mmHg. Subsequently, the abdominal cavity was inspected for metastatic disease or other abnormalities. Under camera supervision, two additional 8 mm trocars were placed for robotic arms, and one port was placed for assisting. The robot was then docked over the patient's head.

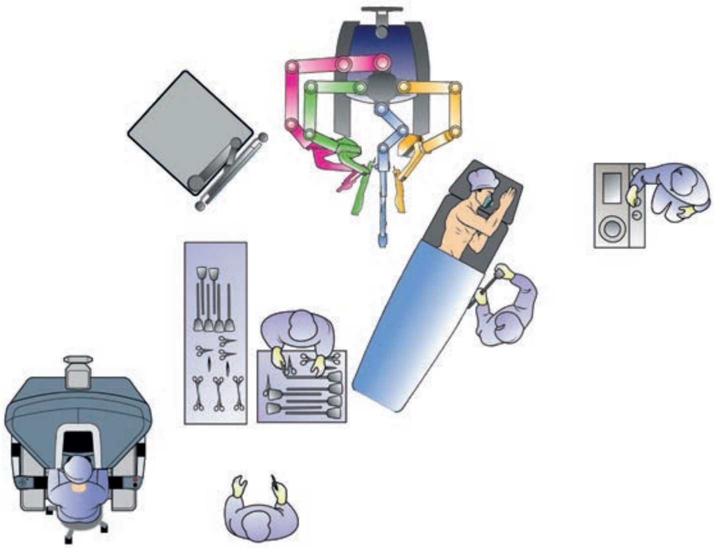

Figure 1. OR set-up in the resection of posterior segment

Room set-up and port placement for resections of posterosuperior segments (7 and 8)

Patients who underwent a resection of a posterosuperior segment were placed in a left lateral position, 15° anti-Trendelenburg to enable optimal mobilization of the right hemiliver and access to the vena cava inferior where appropriate. Subsequently, a 12 mm trocar was placed in the right midclavicular line for camera introduction. Pneumoperitoneum was established, and the abdominal cavity was inspected for metastatic disease or other abnormalities. Under camera supervision, two additional 8 mm trocars were placed for robotic arms, and one port was placed for assistance. The robot was then docked over the patient's right shoulder. (Figure 1, Figure 2)

Procedure

First, the lesion was localized using laparoscopic ultrasound (UST-5550, Aloka ProSound Alpha 10). Subsequently, the liver was mobilized, where necessary. Usually, the liver's capsule and superficial parenchyma were opened using a bipolar dissector (Maryland dissector) and/or monopolar curved scissors. For transection of the liver parenchyma, the EndoWrist One Vessel Sealer or the Maryland bipolar device was used, in conjunction with EndoClips, hem-o-lok clips, sutures, cautery hook, and Endo GIA staplers where appropriate. TachoSil (Takeda Nederland B.V.) was applied to the resection surface where appropriate. Given this initial experience with novel parenchymal transection techniques, a surgical drain was placed near the resection surface with a low threshold.

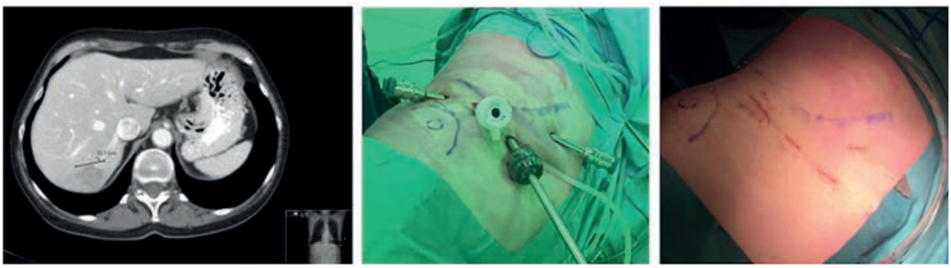

Figure 2. CT scan, port placement and closed incisions of a patient who underwent a resection of a posterosuperior segment

Specimen retrieval

The resected specimens were put in an Endo bag and extracted via the incisions made for port placement. If necessary, those incisions were extended. In the end, the incisions were closed.

Results

Table 1. Patient characteristics and procedures performed

Characteristic	n = ^
Age, median (range), years	69 (34-75)
Male : female	9:7
BMI, median (range), kg/m²	25 (18-33)
Patients with previous abdominal surgery	11
Patients who received chemotherapy preoperatively	6
Patients undergoing major resection (≥4 segments)	0
Patients undergoing minor resection (<4 segments)	15
Resections performed	18
Segment : wedge	4:14
Segmental location	
1	0
2	3
2&3	2
3	1
4a	0
4B	1
5	2
6	1
7	6
8	2

Abbreviations: BMI: body mass index. Legend: ^ reported as ‘n’, unless stated otherwise.

Patient demographics and procedures performed

Patient demographics and procedures performed are summarized in Table 1. Median age was 69 years (range: 34-75). Nine patients were male. Median BMI was 25 kg/m^2 (range: 18-33). Eleven patients had previous abdominal surgery, including two patients who had undergone previous liver surgery. Six patients had received chemotherapy preoperatively. In total, eighteen resections were performed in fifteen patients. Two patients underwent a procedure in which multiple segmentectomies were performed. The majority of the resections were wedge resections, mostly from segment 7.

Pathologic findings

Pathologic findings are summarized in Table 2. The majority of the patients underwent a resection for a malignancy, primarily colorectal liver metastases. One patient had a cholangiocarcinoma (diameter: 25 mm) for which he underwent a resection of segment 4B/5 with en-bloc removal of the gallbladder, resulting in an R0 resection. One patient had a large adenoma; one patient had benign lesions (hemangioma and bile duct adenoma). In twelve patients, the resected specimen contained a metastasis of a colorectal tumor. Median tumor size was 20 mm. In two patients, the surgical margin was positive (R1), both patients underwent liver resection (wedge resection segment 7 and wedge resection segment 2) for colorectal liver metastases.

Operative characteristics

Operative characteristics are summarized in Table 3. Median operative time was 146 min. Median console time was 96 min. Median blood loss was 150 mL. Two patients underwent a laparoscopic bowel resection simultaneously: one patient underwent a sigmoid resection and another patient underwent a hemicolectomy and a robotic cholecystectomy.

One of the procedures had to be converted. This patient had a hepatocellular carcinoma in segment 5. During the procedure, a safe oncologic margin could not be assured robotically due to fibrotic liver parenchyma, and it was decided to convert the procedure to an open procedure, resulting in an R0 resection on histology.

Table 2. Pathologic findings

Characteristic	n = ^
Benign : malignant	2 : 13
Histopathology	
Colorectal liver metastasis	12
Benign (adenoma, hemangioma*)	2
Intrahepatic cholangiocarcinoma	1
Tumor size, median (range), mm	20 (9-57)
Resection margin, median (range), mm	2.5 (0-18)
Positive surgical margin	2

Legend: ^ reported as 'n', unless stated otherwise; * One patient underwent a segment 7 resection for a large adenoma; one patient underwent a segment 2/3 resection for two sub centimeter lesions that were suspect for colorectal liver metastases on CT and MRI scans. Lesions found on pathology, however, were a hemangioma and bile duct adenoma.

Postoperative outcomes

Postoperative outcomes are summarized in Table 3 as well. Seven patients had a complication; three patients suffered from a Clavien-Dindo grade II complication and four patients had a Clavien-Dindo grade III complication. The grade II complications consisted of a patient with a skin rash caused by the surgical drapes, a patient who had urinary retention and a patient with pneumonia. Two patients with a Clavien-Dindo grade III complication underwent percutaneous drainage of a subphrenic fluid collection that turned out to be non-bilious. Both patients underwent resection of a posterior segment (7 respectively 8) and had not received a drain intraoperatively. The third patient who had a grade III complication suffered from an omental herniation through the incision made for the postoperative drain, which had to be closed under local anesthesia. The fourth patient with a grade III b complication suffered from an arterial embolism in one of her lower limbs, which had to be removed surgically.

Median length of stay was four days. There was no mortality in our initial series. All patients were evaluated at our outpatient clinic within one month after discharge from the hospital: all had fully recovered to normal activity, and we observed no wound healing problems.

Table 3. (Post)operative parameters

Characteristic	n = ^
Docking time, median (range), min.	7 (3-13)
Operative time, median (range), min.	146 (60-265)
OR time, median (range), min.	210 (125-400)
Console time, median (range), min.	96 (45-179)
Blood loss, median (range), mL	150 (5-600)
Combined procedure	2
Lap. sigmoid resection	1
Lap. hemicolectomy + cholecystectomy	1
Redo procedure	2
Conversion	1
Patients with postoperative complications	7
CD grade I	0
CD grade II	3
CD grade III a	2
CD grade III b	2
CD grade IV a	0
CD grade IV b	0
CD grade V	0
Length of stay, median (range), days	4 (1-8)
Mortality	0

Abbreviations: OR: operating room; lap.: laparoscopic; CD: Clavien-Dindo.
Legend: ^ reported as 'n', unless stated otherwise.

Discussion

In this study, we present the technique and results of our first sixteen consecutive robot-assisted laparoscopic liver resections. Our results show that robot-assisted laparoscopic minor liver resection of all segments is safe and feasible in selected patients. Indications consisted of colorectal liver metastasis, hepatocellular carcinoma, cholangiocarcinoma, adenoma, and hemangioma.

In addition, eight of our patients underwent a resection of a posterosuperior segment. Conventional laparoscopy is widely used in different gastrointestinal surgical procedures. However, liver surgery is lagging behind. Several studies compared minor and major laparoscopic liver resections with open resections and, in selected patients, laparoscopic liver resection can be performed safely with a significant shorter hospital stay, less blood loss, and similar oncologic outcomes. [5-9]

Still, the percentage of liver resections performed fully laparoscopic in the Netherlands lingers at 11%. [16] Due to the complexity of the vascular and biliary structures in the liver and its tendency to bleed easily when manipulating the tissue, surgeons are probably hesitant to adopt minimally invasive techniques. Moreover, the procedure is associated with a long learning curve. [17, 18] The robotic system has been developed to overcome the limitations of conventional laparoscopy. Compared to conventional laparoscopy, the learning curve of robotic procedures is significantly shorter in other complex gastrointestinal procedures like pancreatic resection. [19] The implementation of minimally invasive approaches to liver resection, nowadays widely performed in an open manner, will more likely be through robotic surgery.

To date, several hundred patients undergoing robot-assisted laparoscopic liver resection have been described in the literature. Most of these patients underwent minor resections of the anterior segments, since most surgeons who start with robot-assisted liver surgery begin with such resections. However, also major resections and resections of the posterosuperior segments are reported. The literature shows that robot-assisted laparoscopic liver resection is feasible and can be safely performed in resections of all segments. Moreover, compared to conventional laparoscopy, it enables a larger percentage of major liver resections to be performed through minimally invasive surgery. [11, 20-22]

In contrast to major liver resections, the size of the incision usually dominates the postoperative recovery in minor resections. [23] Therefore, a minimally invasive approach will probably be the most advantageous in minor resections. Theoretically, the most evident benefit of the robotic system lies in the minor resections of the posterior segments. The possibility to work with angulated instruments makes a robotic system particularly suited for liver resections, which require non-linear manipulation, such as curved parenchymal transection, hilar dissection, and resections of posterosuperior segments. This is in line with our data, which contain eight patients who underwent a robot-assisted laparoscopic liver resection of a posterosuperior segment with adequate outcomes. Moreover, several techniques have been explored in conventional laparoscopy to facilitate posterosuperior resections: hand-assisted laparoscopy or the placement of transthoracic trocars. With the use of a robotic system, none of these are required.

There are a few disadvantages of robot-assisted laparoscopy that must be taken in account. First, the use of current robotic systems is associated with higher costs compared to conventional laparoscopy or open procedures. [10] However, we did not make a direct comparison in cost for use of robotic versus laparoscopic devices in this initial study. Second, robot-assisted laparoscopic liver resection is associated with longer operative times. Studies comparing conventional laparoscopic liver resection with robot-assisted laparoscopic liver resection report a significantly longer operating time in the robotic procedures. Since robot-assisted liver resection is a relatively new procedure, there is little known about the learning curve. Tsung et al. compared ‘early’ with ‘late’ robotic procedures and found a significant decrease of operating time, blood loss, and length of stay over time. Thus, the fact that the learning curve of the robotic procedure is not complete yet must be taken in account. [20, 24]

Conclusion

In conclusion, robot-assisted laparoscopic minor liver resection of all segments is safe and feasible in selected patients. The use of a robotic system may be especially advantageous in resections of the posterior segments. Larger studies are needed to compare robot-assisted laparoscopic liver resection with conventional laparoscopy and the open approach.

Acknowledgements

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Chapter 5

Robotic versus Open Minor Liver Resections of the Posterosuperior Segments:

A Multinational, Propensity Score-Matched Study

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Abstract

Background

Minor liver resections of posterosuperior segments (1, 4A, 7, 8) are challenging to perform laparoscopically and are mainly performed using an open approach. We determined the feasibility of robotic resections of posterosuperior segments and compared short-term outcomes with the open approach.

Methods

Data on open and robotic minor (≤ 3 segments) liver resections including the posterosuperior segments, performed between 2009 and 2016, were collected retrospectively from four hospitals. Robotic and open liver resections were compared, before and after propensity score matching.

Results

In total, 51 robotic and 145 open resections were included. After matching, 31 robotic resections were compared with 31 open resections. Median hospital stay was 4 days (IQR: 3-7) for the robotic group, versus 8 days (IQR: 6-10) for the open group ($p < 0.001$). Median operative time was 222 minutes (IQR: 164-505) for robotic cases versus 231 minutes (IQR: 190-301) for the open cases ($p = 0.668$). Median estimated blood loss was 200 mL (IQR: 100-400) versus 300 mL (IQR: 125-750), respectively ($p = 0.212$). In the robotic group, one patient (3%) had a major complication, versus three patients (10%) in the open group ($p = 0.612$). Readmissions were similar: 10% in the robotic group versus 6% in the open group ($p > 0.99$). There was no mortality in either group.

Conclusion

Minor robotic liver resections of the posterosuperior segments are safe and feasible and display a shorter length of stay than open resections in selected patients at expert centers.

Introduction

Open approach liver resection results in significant morbidity attributable to incisional pain, a large postoperative wound, and pulmonary infections. [1] Recent studies suggest that the introduction of minimally invasive surgery approaches for the liver is improving postoperative outcomes. A meta-analysis of retrospective case series and a recently published randomized controlled trial demonstrated superiority of the laparoscopic approach over open liver resections with respect to postoperative complications and length of stay. [2, 3] However, the laparoscopic approach is limited by anatomic location of certain tumors and the inflexible laparoscopic instruments.

The 2008 Louisville Statement presented the international expert consensus on laparoscopic liver resections selectively recommending the laparoscopic approach as standard practice for resections of anterolateral hepatic segments (2, 3, 4B, 5 and 6). [4] In contrast, this statement, and its 2014 Morioka update, classified resections of the 'difficult' posterosuperior segments (1, 4A, 7, and 8) as 'major liver resection', and recommended against laparoscopic surgery for these segments. [4, 5] The posterosuperior location of segments 1, 4A, 7, and 8 makes these lesions relatively difficult to access with the currently available laparoscopic instruments and was therefore deemed relatively unfit for the minimally invasive approach.

Alternative approaches to facilitate minimally invasive liver resections involving the posterosuperior segments include the laparoscopic hand-assisted transabdominal technique, the laparoscopic transthoracic approach, and the robotic transabdominal approach; [3, 6–10] however, these modified techniques possess their own challenges and potential complications. The hand-assisted transabdominal technique requires an extra incision and is still limited by the compromised visualization. A transthoracic approach potentially increases the risk of seeding of the malignancy to the chest, pleural effusion, and pneumonia. Moreover, a chest tube has to be placed afterwards.

The robotic system offers potential solutions through its more sophisticated features. It provides articulating instruments and a magnified, three-dimensional (3D) view of the operative field, as well as motion scaling and tremor filtering, thereby increasing surgical dexterity. On the contrary, the disadvantages include higher costs of the robot and lack of haptic feedback. [11, 12]

The role of robotic liver resection is undefined. Moreover, little has been published on robotic minor resections of the posterosuperior segments. [13, 14] Parenchymal-sparing resection of the posterosuperior segments often requires a curvilinear transection plane, which can be hard to accomplish with conventional laparoscopy in that difficult location. The authors believe that the robot is particularly well-suited for resections of these segments because of the increased dexterity of the robotic instruments. We hypothesized that robotic minor liver resection of the posterosuperior segments results in shorter hospital stay, with similar perioperative outcomes compared with open resection. We compared surgical parameters and postoperative outcomes between patients undergoing robotic and open minor liver resections of segments 1, 4A, 7, and 8. Data from four expert centers worldwide were retrospectively collected, and groups were compared before and after propensity score matching, to evaluate differences on length of stay as the primary outcome.

Methods

Design and patients

This was a multinational, retrospective cohort study. All adult patients who had a minor robotic liver resection or minor open liver resection including at least one segment or wedge from a posterosuperior segment (1, 4A, 7 and 8) were included. Robotic liver resections performed between January 1st 2009 and December 31st 2016 were collected from three robotic liver surgeons (YF, GC and JH) at four different institutions: City of Hope Comprehensive Cancer Center (YF), Memorial Sloan Kettering Cancer Center (YF), Yonsei University Health System (GC), and the University Medical Center Utrecht (JH). Data on open liver resections performed by various surgeons were collected from three institutions during the same time period (City of Hope Comprehensive Cancer Center, University Medical Center Utrecht, and Yonsei University Health System). (Figure 1)

Patients were excluded if they underwent an additional procedure simultaneously with the liver resection, or if the procedure was a donor hepatectomy or an associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) procedure. Concomitant cholecystectomies, liver biopsies, and en-bloc resection of the diaphragm, retroperitoneum, or adrenal gland were not excluded.

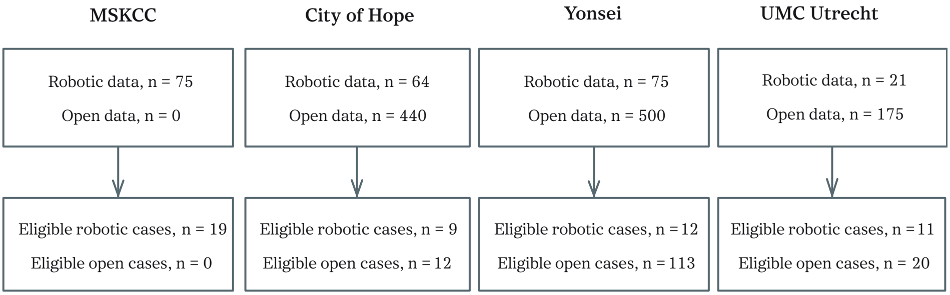

Figure 1. Included patients per hospital (MSKCC: Memorial Sloan Kettering Cancer Center, UMC: University Medical Center)

We adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement. [15]

Definitions

Minor liver resection was defined as resection of three or fewer segments. A wedge resection was counted as a half segment. [16] Liver segments were identified using Couinaud's classification. [17] Segments 1, 4A, 7, and 8 were classified as posterosuperior segments. Operative time was defined as the time from first incision until wound closure. Postoperative complications were scored using Clavien-Dindo's scale for grading postoperative complications; [18] a complication of grade III or higher was considered a major complication. Postoperative parameters were scored up to 90 days after surgery. Conversion was defined as any other laparotomy made than for specimen retrieval. If there were no tumor cells present in the resection plane and within 1 mm of the resection plane, the resection was considered oncologic (R0), however when tumor cells were present in the transection plane or within 1 mm from the resection plane, resection margins were considered microscopically (R1) or macroscopically positive (R2). If multiple tumors were removed, we used the closest margin to determine the R status. Standardized mean differences (SMDs) were defined as the mean difference (mean control group - mean intervention group) divided by the standard deviation of the control group. The participating centers were subdivided into regions: East (Yonsei University Health System) and West (City of Hope Comprehensive Cancer Center, Memorial Sloan Kettering Cancer Center, and University Medical Center Utrecht).

Data collection

Data were collected from existing databases and extracted from patient charts. Baseline characteristics collected consisted of age, sex, body mass index (BMI; in kg/m^2), American Society of Anesthesiologists (ASA) physical status, previous abdominal surgery, and whether the patient received chemotherapy preoperatively. Surgical parameters collected were segments resected, operative time, intraoperative drain placement, blood loss, and conversion. Pathology parameters consisted of histopathology diagnosis, largest tumor size, number of tumors, and margin status. Postoperative outcomes collected were complications, intensive care unit admission, length of hospital stay, surgery-related readmissions, and 30- and 90-day mortality.

Statistical analysis

Patients were divided into two groups based on the surgical approach: robotic versus open liver resection. These two groups were compared for baseline characteristics, as well as primary and secondary outcomes. The primary outcome was length of stay, while secondary outcomes included operative time, blood loss, intraoperative drain placement, major complications, intensive care unit (ICU) admissions, readmissions, margin status, number of tumors, largest tumor size, and 90-day mortality.

Data with a skewed distribution were reported as median with interquartile range (IQR). Continuous data were compared using a Mann-Whitney U test, while categorical variables were compared using a Chi-square test or Fisher's exact test, where appropriate. The analyses were performed as intention to treat.

Propensity score matching

In addition, groups were compared after propensity score matching. Robotic patients were matched to open patients, using a propensity score in a 1:1 ratio, based on BMI, ASA score, previous abdominal surgery, preoperative chemotherapy, age, sex, and region. Propensity scores for undergoing robotic liver resection were calculated using a non-parsimonious multivariable logistic regression model. A patient who had undergone robotic liver resection was matched to the nearest neighbor who had undergone open resection in a random fashion without replacement with a caliper of 0.05. [19, 20] Baseline characteristic imbalances were compared before and after matching using SMDs. We aimed to minimize group imbalances and obtain an absolute SMD smaller than 0.10, with a maximum absolute difference of 0.25 allowed. [20, 21] Matched continuous data were compared using the unpaired two-sided t test or Mann-Whitney U test, where appropriate, and categorical variables were compared using a Chi-square test or Fisher's exact test, where appropriate. Data were analyzed using STATA/MP version 14.2 (StataCorp LLC, College Station, TX, USA). A two-tailed p-value < 0.05 was considered statistically significant.

Zero-truncated negative binominal regression analysis

In addition, we performed a zero-truncated negative binominal regression analysis for length of stay, using the unmatched database. [22] For the multivariate analysis, a mixed-level zero-truncated negative binomial regression to account for clustering of data by region was used. Subsequently, holding all baseline parameters at mean, we predicted length of stay for patients undergoing robotic resection versus patients undergoing open resection.

Ethical approval

The Institutional Review Board of City of Hope Comprehensive Cancer Center approved the study, with a waiver for patient informed consent.

Results

A total of 196 patients were included in our study; 51 patients (26%) had robotic liver resections and 145 patients (74%) had open liver resections. After matching, 31 robotic resections were compared with 31 open resections. Resection types are summarized in Table 1.

Baseline demographics and tumor characteristics

Baseline characteristics and tumor demographics are summarized in Table 2. In the unmatched cohort, the majority of open cases were performed in the East. On the contrary, most of the robotic resections were performed in the West. The open resections were mostly performed for hepatocellular carcinomas, whereas the robotic resections were mainly performed for colorectal liver metastases. After matching, the imbalances between the two groups were fairly reduced, with all SMDs under 0.25.

Table 1. Resection types for the matched and unmatched cohorts

Unmatched cohorts	**Robotic liver resection (n= 51)**		**Open liver resection (n = 145)**	
	Wedge resection	**Segmental resection**	**Wedge resection**	**Segmental resection**
Segment 1, n =	-	-	-	7
Segment 4A, n =	-	-	5	5
Segment 7, n =	8	4	7	7
Segment 8, n =	7	5	7	23
Combination, n = *	27		84	
Matched cohorts	**Robotic liver resection (n= 31)**		**Open liver resection (n = 31)**	
	Wedge resection	**Segmental resection**	**Wedge resection**	**Segmental resection**
Segment 1, n =	-	-	-	1
Segment 4A, n =	-	-	1	-
Segment 7, n =	3	3	2	2
Segment 8, n =	3	2	1	4
Combination, n =*	20		20	

Legend: * Combination of wedge resections/ segmental resections of the posterosuperior segments or in combination with wedge resections/ segmental resections from other segments.

Table 2. Patient demographics and tumor characteristics

	Unmatched			Matched		
Characteristic	**RL (n = 51)**	**OL (n = 145)**	**SMD**	**RL (n= 31)**	**OL (n= 31)**	**SMD**
Age, median (IQR), years	59 (49 - 65)	59 (53 - 67)	0.24	59 (52 - 66)	57 (52 - 63)	-0.18
Male sex, No. (%)	34 (67)	100 (69)	0.05	20 (65)	17 (55)	-0.19
BMI, median (IQR), kg / m2	25 (22 - 28)	24 (22 - 26)	-0.52	25 (22 - 27)	24 (22 - 26)	-0.18
ASA score, No. (%)						
ASA I / II	28 (55)	130 (90)	1.14	20 (65)	19 (61)	-0.07
ASA III / IV	23 (45)	15 (10)	-1.14	11 (35)	12 (39)	0.07
Previous abdominal surgery, No. (%)	32 (63)	54 (37)	-0.53	17 (55)	17 (55)	0.0
Chemotherapy preoperatively, No. (%)	23 (45)	49 (34)	-0.24	14 (45)	12 (39)	-0.13
Region, No. (%)						
West	39 (76)	32 (22)	-1.31	20 (65)	19 (61)	-0.07
East	12 (24)	113 (78)	1.31	11 (35)	12 (39)	0.07
Histopathology, No. (%)						
Colorectal liver metastasis	23 (45)	34 (23)	-0.51	13 (42)	11 (35)	-0.13
Hepatocellular carcinoma	12 (24)	96 (66)	0.90	11 (35)	14 (45)	0.19
Benign	6 (12)	1 (1)	-1.33	2 (6)	1 (3)	-0.18
Intrahepatic cholangiocarcinoma	0 (0)	3 (2)	0.14	0 (0)	0 (0)	N/A
Other metastasis	9 (18)	8 (6)	-0.53	4 (13)	5 (16)	0.09
Combined HCC / CCC	1 (2)	3 (2)	0.01	1 (3)	0 (0)	N/A
Malignancy, No. (%)	45 (88)	144 (99)	1.33	29 (94)	30 (97)	0.18
Lesion origin, No. (%)						
Metastatic	32 (63)	42 (29)	-0.74	17 (55)	16 (52)	-0.06
Primary	13 (25)	102 (70)	0.98	12 (39)	14 (45)	0.13
Benign	6 (12)	1 (1)	-1.33	2 (6)	1 (3)	-0.18

Abbreviations: ASA: American Society of Anesthesiologists; BMI: Body Mass Index; CCC: cholangiocarcinoma; HCC: hepatocellular carcinoma; IQR: interquartile range; OL: open liver resection; RL: robotic liver resection; SMD: standardized mean difference.

Perioperative parameters

Postoperative outcomes are summarized in Table 3. In the matched cohorts, the patients undergoing robotic liver resection displayed a shorter hospital stay compared with patients undergoing open resection (4 days vs. 8 days, respectively; $p < 0.001$), with similar readmission rates. No patients in the robotic group were transferred to the intensive care unit postoperatively, versus 8 patients (26%) in the open group ($p = 0.005$). In the robotic group, 14 patients (45%) received a drain intraoperatively, versus 25 patients (81%) in the open group (p = 0.008). Upon assessment of final pathology, the largest tumor dimension was slightly different (robotic: median 25 mm (IQR: 16-30), versus 30 mm (IQR: 21-41) for the open group). The number of tumors did not differ between the two approaches (robotic: median 1 (IQR: 1-2), versus open: 1 (IQR: 1-2)).

Zero-truncated negative binominal regression analysis

To further explore the results found in the propensity score-matched analysis, we performed a regression analysis, with length of stay as the outcome variable. Results from the univariate and multivariate analyses are summarized in Table 4. After adjusting for all variables expected to influence the outcome in a hierarchical multivariate model, the robotic approach was still significantly associated with a shorter length of stay than the open approach (zero-truncated negative binomial regression coefficient - 0.668, 95% confidence interval (CI): - 0.859, - 0.477; $p < 0.001$). Subsequently, keeping all baseline parameters at the mean, the predicted length of stay for patients undergoing robotic resection was 5 days (95% CI: 4.01 - 6.42), versus 10 days (95% CI: 9.77 - 10.57) for undergoing open resection.

Table 3. Perioperative parameters and surgical outcomes

	Unmatched			Matched		
Characteristic	**RL (n = 51)**	**OL (n =145)**	***p*-value**	**RL (n= 31)**	**OL (n= 31)**	***p*-value**
Operative time, median (IQR), min	198 (141 - 381)	255 (201 - 309)	0.073	222 (164 - 505)	231 (190 - 301)	0.668
Estimated blood loss, median (IQR), mL	180 (100 - 400)	300 (170 - 700)	0.001	200 (100 - 400)	300 (125 - 750)	0.121
Received drain intra-operatively, No. (%)	17 (33)	136 (94)	<0.001	14 (45)	25 (81)	0.008
Conversion, No. (%)	4 (8)	N/A	N/A	2 (6)	N/A	N/A
Major complication, ≥ CD grade III, No. (%)	3 (6)	10 (7)	>0.99	1 (3)	3 (10)	0.612
Major complication, bile leak, No. (%)	0 (0)	3 (2)	0.569	0 (0)	1 (3)	>0.99
ICU admission, No. (%)	0 (0)	11 (8)	0.070	0 (0)	8 (26)	0.005
R1 resection, No. (%)	8 (16)	18 (12)	0.632	4 (13)	7 (23)	0.504
Number of tumors, median (IQR)	1 (1 - 1)	1 (1 - 1)	0.949	1 (1 - 2)	1 (1 - 2)	0.304
Largest tumor size, median (IQR), mm	25 (16 - 31)	25 (20 - 32)	0.316	25 (16 - 30)	30 (21 - 41)	0.032
Length of stay, median (IQR), days	4 (3 - 6)	10 (8 - 13)	<0.001	4 (3 - 7)	8 (6 - 10)	<0.001
Readmission, No. (%)	4 (8)	6 (4)	0.271	3 (10)	2 (6)	>0.99
90-day mortality, No. (%)	0 (0)	0 (0)	N/A	0 (0)	0 (0)	N/A

Abbreviations: CD: Clavien-Dindo; ICU: Intensive Care Unit; IQR: interquartile range; OL: open liver resection; RL: robotic liver resection; N/A: not applicable.

5

Table 4. Univariate and multivariate regression analyses of length of stay

	Univariate analysis			Hierarchical multivariate analysis [a]		
Characteristic	**Coefficient**	**(95 % CI)**	***p*-value**	**Coefficient**	**(95 % CI)**	***p*-value**
Age (continuous)	0.009	(0.001, 0.016)	0.030	0.008	(0.008, 0.008)	<0.001
Gender, male	*reference*					
Gender, female	-0.146	(-0.314, 0.022)	0.089			
BMI (continuous)	-0.016	(-0.040, 0.007)	0.174			
ASA score, I & II	*reference*			*reference*		
ASA score, III & IV	-0.540	(-0.741, -0.338)	<0.001	-0.015	(-0.359, 0.330)	0.934
Previous abdominal surgery, no	*reference*			*reference*		
Previous abdominal surgery, yes	-0.600	(-0.739, -0.462)	<0.001	-0.189	(-0.491, 0.114)	0.221
Chemotherapy preoperatively, no	*reference*			*reference*		
Chemotherapy preoperatively, yes	-0.403	(-0.560, -0.247)	<0.001	-0.013	(-0.334, 0.308)	0.937
Region, East	*reference*					
Region, West	-0.750	(-0.894, -0.607)	<0.001			
Histopathology						
CRLM	*reference*			*reference*		
HCC	0.683	(0.536, 0.830)	<0.001	0.174	(0.169, 0.180)	<0.001
Benign	-0.456	(-0.915, 0.004)	0.052	0	[b]	
CCC	1.100	(0.679, 1.521)	<0.001	0.428	(0.288, 0.568)	<0.001
Other metastasis	-0.142	(-0.420, 0.135)	0.315	-0.063	(-0.064, -0.062)	<0.001
HCC + CCC	0.415	(-0.020, 0.850)	0.061	0	[b]	
Lesion origin						
Primary	*reference*			*reference*		
Metastatic	-0.720	(-0.856, -0.584)	<0.001	-0.206	(-0.246, -0.167)	<0.001
Benign	-1.145	(-1.598, -0.693)	<0.001	-0.241	(-0.343, -0.139)	<0.001
Approach, open	*reference*			*reference*		
Approach, robotic	-0.930	(-1.101, -0.759)	<0.001	-0.668	(-0.859, -0.477)	<0.001

Abbreviations: ASA: American Society of Anesthesiologists; BMI: body mass index; CRLM: colorectal liver metastases; CCC: cholangiocarcinoma; CI: confidence interval; HCC: hepatocellular carcinoma. Legend: [a] data clustered by region; [b] omitted because of collinearity.

Discussion

This multinational, multi-institutional propensity score-matched study demonstrates that robotic minor liver resections of the posterosuperior segments have superior short-term outcomes compared with the open approach. The robotic approach was associated with a shorter length of stay, with no differences in major complication rates and with the ability to achieve negative margins. These findings demonstrate that a robotic approach to minor liver resections of the posterosuperior segments is safe and feasible and may cut the duration of hospital stay by half.

The benefits of conventional laparoscopy over open resections in liver surgery have been shown. [2, 3] Unfortunately, laparoscopic resections of the posterosuperior segments are considered difficult to perform. [23] In several studies on conventional laparoscopic liver resection, resections of the posterosuperior segments are identified as independent predictors for conversion. [24, 25] In addition, laparoscopic resections of the posterosuperior segments were found to have a significantly longer operative time and higher blood loss when compared with laparoscopic resections of the anterolateral segments. [6]

In contrast to conventional laparoscopy, robotic surgery seems to be eminently suited for these resections. The articulating robotic instruments allow the surgeon to operate with more freedom of motion than the human hand. [11] These wristed instruments enable curved transection planes, which are needed in parenchymal-sparing resections of the posterosuperior segments. Previously published case series of robotic liver resections included a small proportion of patients who underwent posterosuperior segments. These demonstrate acceptable outcomes in terms of conversion rate, operative time, and morbidity (reviewed in Nota et al. [14]). One study has been published comparing open and robotic segment 6 and 7 liver resections. [26] Differences found in this study included longer operative time and longer inflow occlusion time for the robotic cases, while length of stay did not differ significantly. However, this study suffered from a small sample size and non-specific eligibility criteria.

The strength of the present study lies in the multi-institutional, multinational character, hereby increasing generalizability of the results. In addition, two different statistical approaches were applied to test the hypothesis and confirm results. The study also made a striking finding on the markedly reduced length of stay, which is a surrogate marker for pain control, mobility, and oral intake in patients' recovery, indicating faster recovery after robotic surgery. Remarkably, several patients included in this study who received robotic minor liver resection had a 1-day hospital stay. Although not measured in this study, there are several explanations for the fact that patients are sent home earlier after robotic liver resection. The absence of a large incision minimizes incisional pain. This results in an improvement of breathing effort and hence a lower risk of pleural effusion and pneumonia, and less need for postoperative oxygen supplementation.

The main limitation of this study lies in the possibility of inherent selection bias due to the retrospective nature of the study. To limit this bias, we kept strict inclusion criteria and aimed to create well-balanced groups using propensity score matching. Although propensity score matching is a well-established method to balance comparative groups, it cannot correct for unmeasured confounders. We performed regression analysis to further confirm the results found in the propensity score-matched analysis. Another limitation to take into account is the fact that certain parameters were not available. Data on preoperative tumor size, proximity of the tumor to vessels, or preoperative Child-Pugh scores were not available, hence could not be incorporated in the regression model to calculate propensity scores. In addition, open cases were only collected from three of four hospitals, thereby potentially introducing bias. However, although raw data on the open resections from this fourth center were not available, the mean length of stay was 7 days for open resections in this center. Thus, this is not very likely to have influenced the results.

There are two main barriers to the adoption of robotic liver resection of posterosuperior segments. First, the robotic operations in this study require a high level of training, dexterity and skill, which is acquired after a significant length of experience in robotic liver resections. The study's surgeries were performed by highly skilled hepatobiliary surgeons. Further studies are needed to investigate the learning curve of robotic liver resection for the next generation of surgeons adopting this technique. Moreover, an international registry of procedures, standardization of techniques, as well as teaching and education within an international focus group for robotic hepato-pancreato-biliary surgery will further aid implementation of these techniques. Second, the costs associated with robotic surgery are currently high. Therefore, robotic hepatectomy should only be embarked upon in institutions with firmly established liver surgery practice and robotic programs covering a wide spectrum of procedures. Interestingly, several companies are expected to bring new surgical robots to the market in the coming years. [27] Hence, competitive pricing will most likely bring down costs. Moreover, a reduced hospital stay, as shown in our study, should also decrease costs.

Conclusion

A robotic approach to minor liver resections of the posterosuperior segments displays several benefits, including a shorter length of stay, than an open approach in selected patients in expert centers. The use of robotic technology possibly extends indications for minimally invasive liver resection.

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Chapter 6

Parenchymal Transection in Robotic Liver Resection:

Results of 70 Resections Using the Vessel Sealer

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Submitted

Abstract

Background

There is no standard technique for transection of the hepatic parenchyma during robotic liver resection. Aim of this study was to describe the outcomes of robotic liver resections during which the Vessel Sealer was used for parenchymal transection.

Methods

This is a *post hoc* analysis of a prospective database. All consecutive patients who underwent robotic liver resection at the Regional Academic Cancer Center Utrecht between August 2015 and January 2019 were included.

Results

A total of 70 robotic liver resections were performed, including 60 minor resections (86%) and ten hemihepatectomies (14%). Five procedures (7%) were converted. Mean parenchymal transection time was 43±26 min. Median blood loss was 150 mL (IQR:40-300). Ten patients (14%) suffered from a major complication, three patients (4%) had bile leakage postoperatively. One patient died from post-hepatectomy liver failure.

Conclusion

Based on the results of this series, consisting of 60 minor liver resections and 10 hemihepatectomies, we conclude that the use of the Vessel Sealer during the parenchymal transection in liver resection is feasible and safe.

Introduction

A minimally invasive approach to liver resection holds several patient benefits, including fewer complications, less blood loss and an enhanced recovery after surgery. [1] Conventional laparoscopy, however, has technical limitations. Laparoscopic instruments have a straight work-axis and, therefore, have limited freedom of movement. To overcome these impairments the surgical robot was introduced. It provides articulating instruments, three-dimensional view and scaled movements. [2, 3] Several studies have shown the safety and feasibility of robotic liver resection. [4]

During liver resection, transection of the hepatic parenchyma forms an essential part of the procedure. Inadequate sealing of vascular and biliary structures can result in bile leakage or bleeding, potentially causing postoperative complications and mortality. Several techniques and devices are developed for parenchymal transection, such as clamp crushing technique, cavitron ultrasonic surgical aspirator (CUSA) (Integra LifeSciences, Tullamore, Ireland), ultrasonic devices, staplers and mono- and bipolar devices. [5, 6] Most of these techniques are developed for, and predominantly used in, open surgery. In laparoscopic liver surgery, the transection is mostly performed using CUSA, sealing devices and staplers. For robotic surgery, it has not yet been determined which device is best suited for parenchymal transection. Currently, the robotic Harmonic Scalpel (Intuitive Surgical, Sunnyvale, California, USA) or robotic bipolar cautery (Maryland Bipolar Forceps, Intuitive Surgical, Sunnyvale, California, USA) are the most frequently reported devices used for parenchymal transection during robotic liver resection. [7] However, the robotic Harmonic Scalpel lacks the ability to articulate and the Maryland Bipolar Forceps seems not optimally suited for larger transection planes.

The EndoWrist ® One™ Vessel Sealer (on the Xi/X robotic systems: EndoWrist ® One™ Vessel Sealer Extend) (Intuitive Surgical Inc., Sunnyvale, CA, USA) is an articulating robotic energy device that seals and cuts vessels up to 7 mm in diameter. The aim of this study is to report the technical details and clinical outcomes of a series of consecutive robotic liver resections during which the Vessel Sealer was used for parenchymal transection.

Methods

Study design and patients

This is a *post hoc* analysis of a prospective database. In addition, recordings of the surgical procedures were reviewed retrospectively for determination of parenchymal transection duration. All consecutive patients who underwent robotic liver resection in the Regional Academic Cancer Center Utrecht (RAKU) (locations: University Medical Center Utrecht and St. Antonius Hospital Nieuwegein) between August 1st, 2015 and January 11th , 2019 were included. Patients were selected for robotic liver resection in a multidisciplinary board meeting. As this case series also reflects a learning curve of robotic hepatectomy starting with easy minor resections and progressing to difficult located minor resections and eventually hemihepatectomy, no uniform inclusion criteria are applicable. In general, exclusion criteria for the robotic approach in this series were: extended liver resection (>4 segments), tumor adjacent to inferior vena cava or hepatic vein insertions, perihilar cholangiocarcinoma, cirrhosis (unless minor/wedge resection).

We adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement.[8] Few of the minor resections of the posterosuperior liver segments have been described earlier within a multi-institutional cohort study, (n=11). [9] The overall initial experience at our center has been published, with surgical outcomes of the first procedures, (n=18). [3, 10]

Definitions

Liver segments were defined using Couinaud's classification.[11] Segments 2, 3, 4B, 5 and 6 were classified as anterolateral segments; segments 1, 4A, 7 and 8 were classified as posterosuperior segments. Minor liver resection was defined as resection of three or less segments, major liver resection as resection of four or more segments. A wedge resection was counted as a half segment.[12] En-bloc resections of the adrenal gland or diaphragm and cholecystectomies were not considered concomitant procedures. Operative time was defined as time from first incision until wound closure. Postoperative complications were scored using the Clavien-Dindo (CD) grading system for postoperative complications. [13] Major complications were defined as CD grade III or higher. Bile leak was defined using the International Study Group of Liver Surgery definition and grading system.[14] Complications were scored during index admission. If a patient was readmitted within ten days after discharge, this readmission was still considered index admission. Conversion was defined as any other laparotomy made than for specimen extraction. Resections were considered radical (R0) if no tumor cells were present in the transection surface and within 1 mm of the transection surface. Resections were considered irradical (R1) if tumor cells were present in the transection surface or within 1 mm of the transection surface. [15] If multiple tumors were resected, the closest margin determined the R status.

Data collection

Baseline characteristics consisted of year of surgery, age, sex, body mass index (BMI), ASA score, previous abdominal surgery, and indication for resection. Data on details of the operation collected were: resection performed, concomitant procedure, operative time, console time, parenchymal transection time, estimated blood loss, conversion, placement of surgical drain, pringle manoeuvre performed, duration of inflow occlusion, epidural analgesia, number of stapler loads used per procedure, type of robotic system, definitive histopathological diagnosis, margin status, and tumor size. Postoperative outcomes were: CD grade III or higher complications, bile leakage, (unplanned) ICU admission, relaparotomy, percutaneous or endoscopic catheter drainage, length of hospital stay, readmission, 30-day mortality, 90-day mortality and trocar herniation during 1 year follow-up.

Statistical analysis

Data with a normal distribution were reported as mean with standard deviation (SD). Data with a skewed distribution were reported as median with interquartile range (IQR). Missing values were reported for each parameter.

Ethical approval

The Medical Ethics Review Committee approved the study protocol with a waiver for informed consent.

Parenchymal transection technique

In the majority of procedures, parenchymal transection began with ultrasound for delineation of the oncologic margin. Either a laparoscopic ultrasound probe was used or a robotic ‘drop-in’ probe (both: Hitachi Aloka Medical Inc., Wallingford, CT, USA). The latter provides more freedom of movement and hence facilitates imaging of the posterosuperior segments more easily. A Pringle manoeuvre was applied when deemed appropriate. The Vessel Sealer (Extend) was combined with the Maryland Bipolar Forceps and Fenestrated Bipolar Forceps. The Vessel Sealer was employed by clamp-crushing thin layers of tissue (as much as possible under direct vision to avoid lacerations of small veins and bile ducts) with subsequent double sealing and cutting, working in layers from superficial to deep in the liver parenchyma as shown previously. [16] Hem-o-lok clips (Teleflex Inc., Morrisville, NC, USA) or laparoscopic Endo GIA (Medtronic, Minneapolis, MN, USA) were used for control of the hepatic pedicles and larger branches of the hepatic veins, where appropriate.

Results

In total, 70 resections were performed in 68 patients. Two patients underwent robotic liver resection twice for recurrent hepatocellular carcinoma.

Patient characteristics

Patient characteristics are summarized in Table 1. The majority of liver resections was performed for colorectal liver metastases, n = 32 (46 %).

Operative characteristics and histopathological outcomes

Details on the surgical procedures and pathology are provided in Table 2. Five procedures were converted to laparotomy, for several reasons: during three cases there was a lack of anatomical overview during transection of the hepatic parenchyma, one patient had severe intra-abdominal adhesions, and in one patient a safe oncologic margin could not be assured robotically.

In all procedures the Vessel Sealer was used for parenchymal transection. In 22 procedures (31%) stapling devices were used as well to control the hepatic pedicles: these resections were left lateral sectionectomies (n=8), left or right

Table 1. Patient characteristics

Characteristic	n (%) ^
Year of surgery	
2014	3 (4)
2015	9 (13)
2016	9 (13)
2017	19 (27)
2018	28 (40)
2019 (up to January 11th)	2 (3)
Age, mean (SD), years	60 (14)
Sex, male	35 (50)
BMI, mean (SD), kg/m²	27 (5)
ASA score [1]	
ASA 1	3 (4)
ASA 2	49 (70)
ASA 3	16 (23)
Previous abdominal surgery	45 (64)
Redo liver resection	6 (9)
Indication for resection	
CRLM	32 (46)
Metastasis, other	7 (10)
HCC	16 (23)
Intrahepatic cholangiocarcinoma	5 (7)
Other	10 (14)

Abbreviations: SD: standard deviation; BMI: body mass index; ASA: American Society of Anesthesiologists; CRLM: colorectal liver metastasis; HCC: hepatocellular carcinoma.
Legend: [1] Two missing values; ^ reported as ‘n (%)’, unless stated otherwise.

Table 2. Operative characteristics and histopathological outcomes

Characteristic	n (%)[^]
Resections performed	
Minor resection solely including anterolateral segments	32 (46)
Minor resection including posterosuperior segments	28 (40)
Major resection (right and left hepatectomy)	10 (14)
Surgical details	
Concomitant procedures	7 (10)
Operative time, mean (SD), min.[2, ~]	160 (78)
Console time, mean (SD), min.[3, *]	111 (69)
Parenchymal transection time, mean (SD), min.[4, *]	43 (26)
EBL, median (IQR), mL	150 (40-300)
RBC transfusions, median (IQR)	0 (0-0)
FFP transfusions, median (IQR)	0 (0-0)
Conversion to laparotomy	5 (7)
Placement of surgical drain	27 (38)
Use of biological agents (TachoSil, Surgicel)*	51 (79)
Pringle manoeuvre performed	31 (44)
Duration of inflow occlusion, mean (SD) min.[5]	41 (15)
Epidural analgesia	20 (29)
Stapler loads used per procedure, median (IQR)*	0 (0-2)
Robotic system used	
da Vinci Si surgical system	55 (79)
da Vinci X surgical system	6 (9)
da Vinci Xi surgical system	9 (13)
Histopathological outcomes	
Definitive diagnosis	
CRLM	31 (44)
Metastasis, other	5 (7)
HCC	15 (21)
Intrahepatic cholangiocarcinoma	4 (6)
Benign	13 (19)
Other	2 (3)
Cirrhosis on final pathology	8 (11)
Radical (R0) resection [#]	42 (76)
Tumor size, mean (SD), mm[&]	37 (26)

Abbreviations: SD: standard deviation; IQR: interquartile range; RBC: red blood cells; FFP: fresh frozen plasma; CRLM: colorectal liver metastasis; HCC: hepatocellular carcinoma. >>

<< **Table 2. Legend:** [2] one missing value; [3] four missing values; [4] twenty missing values; [5] one missing value; ˜ operative time for liver resection, corrected for concomitant procedures; * converted cases excluded; # solely reported for malignancies; & in case of multiple resected tumors, only the largest tumor was included in the calculation; ˆ reported as 'n (%)', unless stated otherwise.

hepatectomies (n=8), resections of the posterior sector (n=3), and resections of segment 7 or 8 (n=3). Overall, median blood loss was 150 mL (IQR: 40-300) and in 51 procedures (79%) biological agents were applied to the resection surface to ensure hemostasis and biliostasis, when deemed appropriate. No technical errors or handling difficulties of the Vessel Sealer were encountered.

Postoperative outcomes

Postoperative outcomes are summarized in Table 3. Ten patients (14%) suffered from a major complication. Three patients (4%) suffered from bile leakage postoperative. Of those, solely two patients needed additional radiological drainage. Median length of hospital stay was four days. In total, 37 patients (53%) were discharged on day 4 or earlier; 12 patients (17%) went home on postoperative day one or two.

One patient died postoperatively due to post hepatectomy liver failure. The patient had a past medical history of hepatitis B, no signs of cirrhosis or portal hypertension in preoperative hepatology evaluation, and underwent right hepatectomy for a hepatocellular carcinoma. Due to the lack of anatomical overview during parenchymal transection, the procedure was converted to open hemihepatectomy. Postoperatively, the patient suffered from grade C post hepatectomy liver failure progressing to multiple organ failure and death on postoperative day 12. Definitive pathology showed a hepatocellular carcinoma as well as liver cirrhosis.

Discussion

In this study we report the surgical details and clinical outcomes of 70 consecutive robotic liver resections in which the Vessel Sealer was used for parenchymal transection. Our results demonstrate that the use of this device facilitates safe transection of the hepatic parenchyma, without compromising postoperative clinical outcomes. No postoperative bleedings occurred and only three patients (4%) suffered from bile leakage postoperatively.

Table 3. Postoperative outcomes

Characteristic	n (%) ^
Major complication	10 (14)
Clavien-Dindo grade III a/b	7 (10)
Clavien-Dindo grade IV a/b	2 (3)
Bile leakage	3 (4)
ICU admission	5 (7)
Unplanned ICU admission	3 (4)
Relaparotomies	0 (0)
Minimally invasive drainages	5 (7)
Length of stay, median (IQR), days	4 (3-6)
Readmission within 10 days	4 (6)
Readmission within 90 days	6 (9)
30-day mortality	1 (1)
90-day mortality	1 (1)
Trocar herniation within one year after surgery requiring surgical intervention	2 (3)

Abbreviations: ICU: Intensive care unit; IQR: interquartile range. Legend: ^ reported as 'n (%)', unless stated otherwise.

Over the past decade, robotic surgery has become an important alternative to conventional laparoscopy. Recently, a nationwide trend in the US towards an increase of the use of robotic surgery has been observed for pancreatoduodenectomy, whilst the number of conventional laparoscopic pancreatoduodenectomies performed decreased.[17] This finding supports the hypothesis that robotic surgery might be better suited (and more widely implemented) than conventional laparoscopy for complex procedures, such as pancreatic resection or liver resection.

Since the use of robotic technology in liver resection is gaining momentum, new techniques and devices for parenchymal transection have emerged. Initial series on robotic liver resection mostly report the use of the robotic Harmonic Scalpel or the Maryland Bipolar Forceps for transection of the parenchyma.[7]

Other currently available devices include: PK Dissecting Forceps (Intuitive Surgical, Sunnyvale, California, USA), EndoClips, robotic stapler, and the Vessel Sealer. [18] The Harmonic Scalpel, however, lacks the ability to articulate. The Maryland Bipolar Forceps and the PK Dissecting Forceps provide meticulous dissection, but these instruments appear inefficient for larger transection planes. EndoClips provide reliable ligation of vessels and bile ducts, though do not seem efficient for larger transection planes as well. Robotic staplers facilitate reliable sealing, but are expensive. Few cases using the Vessel Sealer for transection of the parenchyma during robotic liver resection have been reported by Kingham et al., however, no separate outcomes were reported for the different transection techniques used in this study. [19]

The results in our study demonstrate that the use of the Vessel Sealer is feasible and safe during robotic liver resection. Only ten patients (14%) suffered from a major complication, from which one patient died. However, this patient suffered from post hepatectomy liver failure, which is most likely a consequence of the extent of the resection rather than of the parenchymal transection technique chosen. Three patients (4%) suffered postoperatively from bile leakage, which is comparable to large series on open and laparoscopic liver resection. [20-23] The R1 resection rate in our series (defined as a surgical margin of < 1 mm) appears to be relatively high (24%). However, studies show that R1 resection for colorectal liver metastases can be considered acceptable. [24, 25] In addition, in our initial series, robotic manipulation of the liver tissue during resection may have caused inadvertent laceration in the specimen contributing to the number of R1's on final pathology in several cases.

Several limitations must be taken into account for this study. First, the patients who underwent robotic liver resection in this study were selected. Patients with tumors adjacent to the hepatic vessels, patients who underwent extended hepatectomies (≥ 6 segments) or patients who had a past medical history of extensive abdominal surgery, were in general not deemed fit for a robotic approach. Although our resections might not fully represent the entire spectrum of liver resections, there were ten major resections performed (14%) and indications varied widely, also including patients with cirrhosis (11%). Moreover, 45 patients (64%) were selected who underwent previous abdominal surgery, including previous liver surgery in six patients. Second, some surgeons consider the tip of the Vessel Sealer to be too bulky and prefer a more refined instrument for transection of the parenchyma and dissecting out hepatic structures. The updated version of the Vessel Sealer, the Vessel Sealer Extend, however, has a slimmer jaw profile and therefore allows for more delicate dissection. Third, the retrospective nature of the study holds an inherent risk of bias.

Conclusion

Based on the results of this series, consisting of 60 minor liver resections and 10 hemihepatectomies, we conclude that the use of the Vessel Sealer during the parenchymal transection in liver resection is feasible and safe.

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Chapter 7.1

Video Chapter Robotic Right Hepatectomy for a Central Liver Tumor:

a Video of the Surgical Technique

7

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Surgical Oncology
2019;30:108

Abstract

Background

Robotic surgery is gaining momentum in liver resection. Instrumentation of the surgical robot is articulated, movements are scaled and the view of the operative field is three-dimensional and magnified. [1, 2] Thus, these technical enhancements allow for a more precise dissection and curved work axes, as needed in liver resection. Aim of this video was to demonstrate the feasibility of fully robotic right hepatectomy with dissection of the variant right hepatic pedicles for a centrally located liver tumor.

Methods

This video illustrates robotic right hepatectomy in a 77-year-old male. A liver tumor in segment 5/8 with concurrent biliary dilation was detected on a CT-scan made in the course of his cardiac history. An additional MRI scan suggested the diagnosis of hepatocellular carcinoma or intrahepatic cholangiocarcinoma for which a right hepatectomy was indicated.

Results

After anesthesia, the patient was placed supine on a split-leg table in anti-Trendelenburg and left lateral tilt position. Four robotic trocars were placed and the da Vinci Xi robotic system was docked. Two laparoscopic ports were placed for tableside assistance. Right hepatectomy was performed including separate dissection of the posterior and anterior pedicles. The robotic Vessel Sealer was employed as main parenchymal transection device. Postoperative hospital stay was unremarkable. The patient was discharged on postoperative day 6.

Conclusion

This video illustrates the feasibility of a robotic approach to right hepatectomy. The increased surgical dexterity, as provided by the articulating robotic instrumentation, allows for precise dissection of the liver hilum, as needed in resection of centrally located tumors.

Video

QR code to video

Link to video

https://www.sciencedirect.com/science/article/pii/S0960740419302348?via%3Dihub#mmc2

or

https://player.vimeo.com/external/338398127.hd.mp4?s=5fb7233ca11e355140aea1bfbe5b84bee39399f0&profile_id=174

or

https://tinyurl.com/CNota-Video72

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Chapter 7.2

Video Chapter Robotic Liver Resection of Segment 7:

a Step-By-Step Description of the Technique

7

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Submitted

Abstract

Background

Robotic surgery is increasingly employed in complex procedures such as liver resection. Minor resections of the posterosuperior segments might benefit in particular from a robotic approach, since the size of the incision dominates the postoperative recovery rather than the extent of the resection. [1] We aimed to provide a standardized, step-wise guide to robotic liver resection of segment 7.

Methods

This video illustrates, step-by-step, robotic segment 7 resection. Patients are placed in left lateral position, slight anti-Trendelenburg. Three robotic ports are used and one conventional laparoscopic port is placed for bedside assistance. Next, segment 7 is mobilized. Intraoperative ultrasound is used to delineate the tumor and ensure a safe oncologic margin. The EndoWrist ® One™ Vessel Sealer (Extend) (Intuitive Surgical Inc., Sunnyvale, CA, USA) is used for transection of the hepatic parenchyma, combined with a bipolar Maryland Forceps (Intuitive Surgical, Sunnyvale, California, USA). Hem-o-lok clips (Teleflex Inc., Morrisville, NC, USA) or laparoscopic staplers (Medtronic, Minneapolis, MN, USA) are used to control the hepatic pedicle. A pringle manoeuvre is applied when deemed appropriate. To ensure hemostasis and biliostasis, TachoSil (Takeda Nederland b.v. Takeda, Zurich, Switzerland) is applied to the resection surface. The specimen is extracted through an enlarged trocar incision.

Results

This video illustrates robotic liver resection of segment 7 in a 72-year-old male with a past medical history of colorectal cancer. New, resectable liver metastases were detected during follow-up. The procedure was completed fully robotically. No postoperative complications occurred and the patient was discharged on postoperative day one.

Conclusion

This video provides a step-by-step guide to robotic liver resection of segment 7.

Video

QR code to video

Link to video

https://player.vimeo.com/external/370676150.hd.mp4?s=642c03de6a87d1aa96709a09fe2d10c54f4fa086&profile_id=174

or

https://tinyurl.com/CNota72

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Part 2

Robotic Pancreatic Surgery

Chapter 8

The Development of a Robotic Pancreas Program:

The Dutch Experience

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Abstract

Robot-assisted surgery has been developed to overcome limitations of conventional laparoscopy aiming to further optimize minimally invasive surgery. Despite the fact that robotics already have been widely adopted in urology, gynaecology, and several gastrointestinal procedures, like colorectal surgery, pancreatic surgery lags behind. Due to the complex nature of the procedure, surgeons probably have been hesitant to apply minimally invasive techniques in pancreatic surgery. Nevertheless, the past few years pancreatic surgery has been catching up. An increasing number of procedures are being performed laparoscopically and robotically, despite it being a highly complex procedure with high morbidity and mortality rates. Since the complex nature and extensiveness of the procedure, the start of a robotic pancreatic program should be properly prepared and should comply with several conditions within high-volume centers. Robotic training plays a significant role in the preparation. In this review we discuss the different aspects of preparation when working towards the start of a robotic pancreas program against the background of our nationwide experience in the Netherlands.

Introduction

Minimally invasive pancreatic surgery is gaining popularity worldwide. Although less overwhelming compared with other subdisciplines of gastrointestinal surgery, the portion of pancreatic resections performed minimally invasive is clearly increasing. [1] To date only non-randomized studies are available comparing open resection with minimally invasive techniques in pancreatic surgery. These studies suggest several benefits of minimally invasive surgery including less blood loss and shorter hospital stay. [2-5] Currently, multicenter randomized controlled trials are being carried out in the Netherlands comparing open resection with a minimally invasive approach, for both distal pancreatectomy and pancreatoduodenectomy. [6, 7]

Despite its potential benefits, conventional laparoscopy has several technical drawbacks and is, independent of the outcomes of trials, technically more demanding than open surgery. Rigid (i.e. non-articulating) instruments and uncomfortable ergonomics may hinder the broader implementation of minimally invasive pancreatic surgery.

In 2000, the first commercially available robotic system was introduced to overcome these limitations. This robotic system aims to combine the benefits of open and conventional minimally invasive surgery by providing a three-dimensional, magnified view of the operative field with intra-abdominal articulating instruments, thereby increasing surgical dexterity. [8] Potentially, the use of the robotic system enables a larger proportion of pancreatic surgeries to be performed minimally invasively, since the technical benefits of the robot may especially be advantageous in constructing anastomoses during a Whipple procedure. Moreover, ergonomics are improved and the use of robotics in minimally invasive surgery potentially shortens the learning curve compared to conventional laparoscopy, as previously shown in different procedures. [9, 10]

Still, pancreatic surgery remains highly complex and is associated with significant morbidity and mortality rates. [11-13] Therefore, when starting a robotic program for pancreatic surgery, it should be well prepared and several conditions must be met prior to performing the first procedures. Training of a dedicated multidisciplinary team should play a key role in the set-up. However, specific training programs for teams performing robotic pancreatic surgery are still scarce.

In the Netherlands, surgeons have been performing laparoscopic pancreatic surgery sporadically for over ten years. [1] In 2012, the first robot-assisted distal pancreatectomies were performed and last year the first robot-assisted pancreatoduodenectomies were performed in the University Medical Center Utrecht (UMC Utrecht) after following the University of Pittsburgh Medical Center (UPMC) training program. Next, this program made available nationwide by the Dutch Pancreatic Cancer Group (DPCG), similar as was done previously for laparoscopic pancreatic surgery. [1] Other centers, including the Erasmus Medical Center Rotterdam, recently followed the program. In this review we discuss the steps we took on our road to our first successful robot-assisted pancreatoduodenectomy.

The start of the program

With support of the department and hospital leadership, programs should be started only in high-volume centers. A recent study demonstrated that centers with an annual volume less than 22 minimally invasive pancreatoduodenectomies have inferior outcomes. [14] A team of dedicated members from several departments should be composed at the start of the project. A complete team should include experienced pancreatic surgeons, operating room nurses, anesthesiologists, and anesthesiology nurses.

Team: experienced HPB surgeons/pancreatic surgeons

Pancreatic resections are complex procedures, with considerable morbidity and mortality. Performing these procedures in a minimally invasive manner makes it even more complex. We are convinced that extensive experience in open hepato-pancreato-biliary (HPB) surgery is essential when setting up a robotic program. All surgeons involved in our project had extensive experience in open pancreatic surgery. Besides that, the surgeons enrolled in the robotic pancreas program had prior experience with conventional laparoscopic pancreatic surgery or had experience with other robotic procedures, like liver resection. The robotic pancreatoduodenectomy is mostly performed by two surgeons. Thus, preferably, the same surgeons should be involved in the set-up.

Team: dedicated scrub nurses

All participating scrub nurses were dedicated HPB scrub nurses with extensive experience in open HPB surgery. Besides this, they had extensive experience in high complex robotic surgery (esophagectomies, liver resections, and/or donor nephrectomies). Especially the combination of these two ensures a short learning curve and a rapid build-up of experience.

Team: anesthesiology

Dedicated HPB anesthesiologists and anesthesiology nurses are needed to ensure fast standardization of the procedure. Performing a pancreatoduodenectomy robotically requires several adjustments, also from the anesthesia team. Airway access can be suboptimal with a docked robot (not with the da Vinci Xi system), sequential compression devices are necessary since the patient will be lying in anti-Trendelenburg for a significant period of time and extra-long IV lines may be necessary to obtain enough space for the robotic system.

Equipment

Alongside the dedicated team, the right equipment should be available. In the Netherlands, most centers started with robotic pancreatic surgery relatively late compared to other robotic procedures; therefore most of the needed equipment and instruments were already available. Intuitive Surgical's da Vinci S system, as well as the da Vinci Si system and da Vinci Xi system are suited for the robotic pancreatoduodenectomy (Intuitive Surgical, Sunnyvale, California, USA). In our experience most of the needed instruments were already available in the hospital. Although not used in open pancreatic resections, instruments like laparoscopic liver retractors, silk sutures, V-Loc sutures and beanbags were already available.

Training

Training in minimally invasive surgery has been shown beneficial. [1, 15, 16] However, specific training programs for robotic pancreatic surgery are not widely available yet. When starting up a robotic program for a complex procedure like a pancreatic resection, surgical training should have a significant share in the preparation. Especially reconstruction following a pancreatoduodenectomy requires advanced suture skills and therefore should be trained extensively.

In the Netherlands, the nationwide LAELAPS training program for laparoscopic pancreatic surgery was initiated in 2013. [1] In this program, surgeons were trained for laparoscopic distal pancreatectomy. Training consisted of video training, detailed description of the technique/procedure and on-site proctoring by an experienced laparoscopic pancreatic surgeon. In procedures performed after the training program, a significant lower conversion rate (38% to 8%), less blood loss and a shorter hospital stay were observed compared to procedures performed before the training program. This program showed that training is feasible, beneficial and was followed by a 7-fold increase the proportion of distal pancreatectomies performed laparoscopically in the Netherlands. [1] In 2016, the LAELAPS-2 program for laparoscopic pancreatoduodenectomy was started.

As a continuation of the successful LAELAPS-1 and -2 programs and after the success of the transatlantic implementation of the UPMC training program, a nationwide program for the safe introduction of the robot-assisted pancreatoduodenectomy in the rest of the Netherlands was developed in 2016: LAELAPS-3. The aim of this program was to introduce robotic pancreatoduodenectomy without a learning curve in complications, but only a learning curve in operating time. This program was set up in close collaboration with Dr. Herbert Zeh and Dr. Melissa Hogg, initiators of the UPMC robotic pancreas program and the specific training program on robot pancreatic surgery, respectively. Their program was the basis of the LAELAPS-3 program.

Nationwide training program: LAELAPS-3

Training in LAELAPS-3 consists of simulation exercises, suture exercises, practicing anastomoses on artificial organs, watching multiple video recordings of all phases of the procedure and on-site proctoring of the first procedures by a UPMC surgeon. Currently, surgeons in four hospitals have performed their first robotic pancreatoduodenectomy.

Basic robot training course

Prior to starting robotic surgery in general, there are several official courses available one can follow in order to get familiarized with the basic use of the robotic system. Although this is not part of the official LAELAPS-3 training program, every surgeon involved in this program is required to have basic knowledge on the use of the robot, preferably obtained after following one of the official courses, e.g. Intuitive Surgical's the da Vinci® Technology Training Pathway. [17]

Simulation training

The first steps of the program consist of simulation exercises. These exercises can be done on a training robot (e.g. Mimic®, Mimic technologies, Seattle, Washington, USA) or on a da Vinci robotic system with the use of a da Vinci Skills Simulator, or 'backpack' simulator (Intuitive Surgical, Sunnyvale, California, USA).

Figure 1. The box trainer

In the LAELAPS-3 program simulation is subdivided in three categories: pretest, curriculum and posttest. Pretest and posttest consist of the same exercises: several basic exercises on a Mimic or with help of the backpack simulator and three different box trainer exercises. (Figure 1) The middle part of the simulation training is the 'curriculum'. [18] These are 25 exercises on a Mimic or backpack simulator in which one must obtain a predetermined 90% level of proficiency before passing. Every exercise is taped and scored by the coordinators of the training program using a standardized scoring form.

Advanced suturing and anastomoses training on artificial tissue

In the reconstruction phase of a pancreatoduodenectomy, precise suturing is required for the pancreato-, hepatico- and gastrojejunostomy anastomoses. Fortunately, the suturing within these anastomoses can be practiced in a simulated situation. [19] Hence, simulation plays an important role in this second step of the training program. One will start with basic suture exercises on a piece of artificial human skin. These exercises can be done on a training robot (if available) or in the OR. Next, the anastomoses of the Whipple procedure (e.g. pancreaticojejunostomy and hepaticojejunostomy) are performed on artificial tissue. (Figure 2) All exercises are recorded and scored by the coordinators of the LAELAPS-3 program. Different aspects of a surgeon's performance are scored using the objective structured assessment of technical skills (OSATS) method, e.g. gentleness, time, flow of the exercise, and instrument handling. [20] Currently, these scores are collected in prospective databases for research purposes.

Video training

Although the reconstruction phase of the Whipple procedure can be practiced in a simulated setting easily, this differs for the resection phase of the procedure. The resection phase is trained in our program by a recommended six hours of video observing. These videos are provided on an online platform by UPMC. The platform includes full videos of resections for various pathologies, as well as multiple videos of each phase of the resection and reconstruction. Especially for the resection phase of the procedure, we are convinced that extensive experience in open pancreatic surgery will simplify this part of the operation.

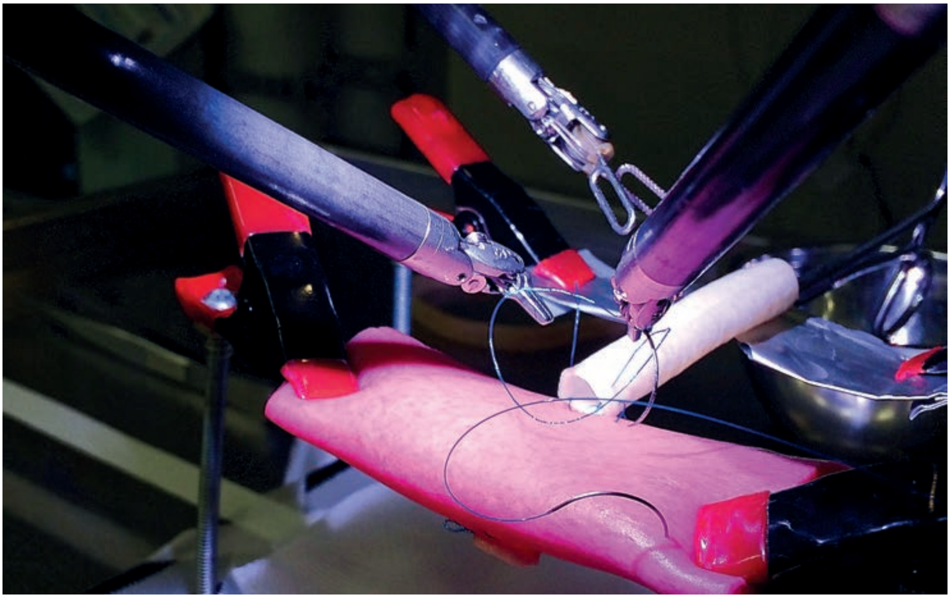

Figure 2. Construction of a hepaticojejunostomy on artificial organs

Proctoring of the first procedures

Once the official LAELAPS-3 training program has been successfully completed, the first procedures can be planned. Despite extensive training, the robotic Whipple remains a technically challenging procedure. Hence a more experienced robotic pancreatic surgeon should proctor the first cases. A proctor is more experienced and better aware of the potential obstacles that can be encountered and the possible solutions. Moreover, the direct help of the proctor ensures that the procedure will be finished in a reasonable amount of time.

In our nationwide training program we aim to strategically plan the training sessions for the participating surgeons, so their first procedures can be preferably planned during a single week. In this week, a proctor from UPMC visits the Netherlands to attend the first procedures in different hospitals. The UMC Utrecht has performed over 15 robotic Whipple procedures at this moment and therefore will accompany the proctoring process once the initial learning curve of 20 procedures has been completed.

Patient selection

After finishing training, the most important next step is the initial patient selection. Currently, no guidelines exist for patient selection for minimally invasive pancreatoduodenectomy. In our nationwide experience, patients who underwent pancreatic radiotherapy, extensive upper abdominal surgery, have chronic pancreatitis, who have medical conditions that preclude them from lying in anti-Trendelenburg or who were expected to have problems tolerating pneumoperitoneum, were excluded for undergoing robotic pancreatic resection.

Besides these general exclusion criteria, there are a few other patient and tumor characteristics that should be taken into account. First, body mass index (BMI). There is no consensus currently on ideal BMI for robotic pancreatic surgery. In fact, gaining adequate working space can be difficult when operating on a patient with a very low BMI. On the other hand, in patients with a significantly higher BMI, it can be troublesome to reach the pancreas with the robotic instruments. When starting up a program, a BMI between 20 and 35 kg/m^2 should be considered for robotic pancreatic surgery. These guidelines can be extended after increased experience. In the ongoing Dutch trials on minimally invasive pancreatic surgery patients with a BMI over 35 are excluded. [6, 7]

Tumor characteristics should be considered as well, especially in the beginning of one's learning curve. Patients with recurrent acute or chronic pancreatitis, tumors with abutment of the portal vein or superior mesenteric vein that may require vascular reconstruction and large (duodenal) tumors (>6 cm) should not be selected. Although vascular resections have been demonstrated to be safe and feasible in robotic pancreatoduodenectomy, this demands a certain level of expertise and experience. [21, 22] When selecting patients for a robotic pancreatoduodenectomy, benign lesions (e.g. IPMN or ampullary adenoma) or patients who have a dilated pancreatic duct and/or bile duct, are eminently suited for the first procedures.

Tips, tricks and pitfalls

The vital factor in making a success of your robotic program is team work. Dedication of surgeons, OR staff and the anesthesia team is key. The same team should be involved in, at least, the first ten procedures. Additionally, robotic experts from other departments should be consulted during your start-up. Prior to the first procedure, we recommend doing a comprehensive run-through the protocol with the entire team. In this way, the availability of the right instruments is assured and everybody is well aware of one's tasks and attuned to each other.

Second, one should take their time for training and getting the team ready for the first procedure. Although it can be tempting to quickly go through training and start the program, one should not rush into it. This also applies to surgeons who are experienced in pancreatic surgery. Rushing into a procedure like a robotic pancreatic resection can potentially jeopardize patient safety.

Lastly, for the safe set-up and expansion of the program an adequate learning curve is essential. Therefore, when starting your program, OR time and robotic availability should be assured for the upcoming months.

Evolution of robots, tools and education

As the Intuitive robotic systems evolve, and new entries from other companies come into the market, it is likely that complex operations such as pancreato-duodenectomy will get easier, safer, and be accessible to a wider fraction of surgeons. With the advent of the Xi robot for example, multi-quadrant surgery no longer requires moving the robot, but simply retargeting the instruments and redocking from the robot in the same location. [23] With ever improving stapling and vessel sealing capabilities, the safety of the operation will undoubtedly improve. We will need to be sure educational materials, such as Atlases of robotic surgery are widely available for reference and for ongoing refresh for clinical practice. [24] Some professional societies, such as the Society of American Gastrointestinal and Endoscopic Surgery (SAGES), in preparation for widespread adoption of robotic surgery and complex robotic surgery, have begun publication of such atlases.

Conclusion

In conclusion, if well prepared, robotic pancreatoduodenectomy can be safely implemented within high-volume centers. Studies have shown promising results (e.g. reductions in major complications, less blood loss) of the use of a robotic system in pancreatic surgery. [2] In order to safely start a robotic program for pancreatic surgery, several components are necessary, including a dedicated team, prior experience with pancreatic surgery and minimally invasive surgery and first and foremost structured training. In our opinion, these factors are essential for the safe and successful implementation. Even though structured training programs for robotic pancreatic surgery are scarce nowadays, it is to be expected that training will be become broader implemented and more important in the future.

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Chapter 9

Stepwise Implementation of Robotic Surgery in a High Volume HPB Practice in The Netherlands

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Submitted

Abstract

Background

The number of robotic hepato-pancreato-biliary (HPB) surgeries is increasing. Although several consensus papers have been published on how to start a robotic program from a technical viewpoint, actual implementation of robotic surgery in the daily practice of an HPB surgeons' group has not been addressed. Aims of this study were to describe the stepwise implementation and expansion of robotic HPB surgery in a high volume center in the Netherlands and to analyze clinical outcomes of all robotic liver resections and robotic pancreatoduodenectomies performed within this program.

Methods

After proctoring by expert international surgeons, HPB surgeons were introduced to robotic liver resection and robotic pancreatoduodenectomy in a stepwise fashion. Data from two prospective databases containing all consecutive patients who underwent robotic liver resection or robotic pancreatoduodenectomy in our center between August 1st , 2015 and March 1st, 2019 were analyzed *post hoc*.

Results

In total, 77 consecutive robotic liver resections and 68 consecutive robotic pancreatoduodenectomies were performed. Five surgeons were consecutively introduced to robotic HPB surgery. Mean operative time for robotic liver resection was 160±78 minutes. Mean operative time for robotic pancreatoduodenectomy was 420±67 minutes. Operative times remained stable over time and were not affected by the introduction of new surgeons.

Conclusion

Stepwise implementation and expansion of robotic HPB surgery within one center is feasible and associated with good clinical outcomes. Despite introducing new surgeons to the technique, operative times, an indicator of the learning process, remained stable over time.

Introduction

Over the past few years minimally invasive surgery (MIS) has been gaining ground in the field of hepato-pancreato-biliary (HPB) surgery. Implementation of MIS in HPB surgery has been relatively slow as compared with other procedures., This may be explained by the complexity of these procedures and the high risk of complications. Nevertheless, the percentages of liver resections and pancreatic resections that are being performed through MIS have been gradually increasing and several (non-)randomized studies have demonstrated potential advantages of a minimally invasive approach to both liver and pancreatic resections, such as enhanced recovery after surgery and fewer (severe) complications. [1-5] Initially, when MIS in HPB surgery was in its infancy, most of the procedures were performed through conventional laparoscopy. [6-8] However, due to the technical limitations of conventional laparoscopy, robotic surgery is increasingly performed. A recent study on trends in minimally invasive pancreatoduodenectomy in the United States showed an overall decrease in the use of conventional laparoscopy and an increase in the use of robotics over the past few years. [9] The same trend has been observed in several other surgical specialties. [10] Robotic surgery provides scaled movements, magnified three-dimensional vision, articulating instrumentation and improved ergonomics for the surgeon, compared to conventional laparoscopy.[11]

Several consensus meetings have been held on the implementation of both minimally invasive liver surgery and pancreatic surgery. Papers derived from these meetings (e.g. The Louisville Statement, Morioka Consensus Conference, Southampton Guidelines, Coimbatore Summit Statements, and the recent Miami International Evidence-Based Guidelines) highlight the importance of training (e.g. basic courses on robotics, skills lab etc.), proctoring and case selection when starting up a robotic (or laparoscopic) HPB program. [12-16] The further expansion of robotic HPB surgery within a larger team of HPB surgeons within one center, has not been addressed. Hence, the aim of this study was twofold. First, to describe the stepwise implementation and expansion of robotic HPB surgery in a high volume expert center in the Netherlands with five HPB surgeons, aimed to create a stable and lasting robotic HPB program. Second, to provide a summary of the surgical details and clinical outcomes of all robotic liver resections and robotic pancreatoduodenectomies performed within this program.

Materials and Methods

Study design and patients

This is a *post hoc* analysis of two prospective databases containing all consecutive patients who underwent robotic liver resection or robotic pancreatoduodenectomy in the Regional Academic Cancer Center Utrecht (RAKU) (locations: University Medical Center Utrecht and St. Antonius Hospital Nieuwegein) between August 1st , 2015 and March 1st , 2019. Patients were selected for robotic liver resection or robotic pancreatoduodenectomy in a multidisciplinary oncology board, attended by surgeons, radiologists, medical oncologists, radiation oncologists, pathologists and hepatologists. Patients undergoing liver resection were generally deemed unsuitable for a robotic approach if they had to undergo extended resections (≥ 5 segments) or if the tumor necessitated central dissection. Patients undergoing pancreatoduodenectomy were not selected for a robotic approach if the tumor had vascular contact, if the patient had a history of severe pancreatitis or if the patient had undergone previous extensive abdominal surgery. We adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement. [17]

Data collection

Baseline characteristics consisted of age, sex, Body Mass Index (BMI), American Society of Anesthesiologists (ASA) score, previous abdominal surgery and indication for resection. Data on details of the operation and postoperative course collected were: operative time (min), estimated blood loss (EBL), conversion, bile leakage, unplanned Intensive Care Unit (ICU) admission, length of stay (days), 30-day or in-hospital mortality. In addition, for liver resection, type and extent of resection were collected. For pancreatoduodenectomy, post-pancreatectomy hemorrhage (PPH), postoperative pancreatic fistula (POPF) and delayed gastric emptying (DGE) were collected.

Definitions

Operative time was defined as time from first incision to wound closure. Operative time was corrected for any additional procedures performed and hence solely reflects the operative time of the robotic HPB procedures.

Postoperative complications were scored during index admission. If a patient was readmitted within ten days after discharge, this readmission was still considered index admission. Conversion was defined as any other laparotomy made than for specimen extraction. Bile leakage was defined and graded using the International Study Group on Liver Surgery (ISGLS) definition.[18] Liver segments were defined using Couinaud's classification. [19] Segments 2, 3, 4B, 5 and 6 were classified as anterolateral segments; segments 1, 4A, 7 and 8 were classified as posterosuperior segments. Minor liver resection was defined as resection of three or less segments, major liver resection as resection of four or more segments. A wedge resection was counted as a half segment. [20] Pancreas-specific complications such as PPH, POPF and DGE were defined and graded using the International Study Group in Pancreatic Surgery (ISGPS) definitions. [21-23]

Statistical analysis

Data with a normal distribution were reported as mean with standard deviation (SD). Data with a skewed distribution were reported as median with interquartile range (IQR). Missing values were reported for each parameter.

Set-up of the program

An extensive description for both the set-up of the robotic liver surgery program and the set-up of the robotic pancreatoduodenectomy program has been published before. [24, 25] Robotic distal pancreatectomy was performed as well at our center, but with lower volume than hepatectomy and pancreatoduodenectomy. Therefore, data on distal pancreatectomy are not included in this study.

Surgical technique - Robotic liver resection

Patient undergoing resection of the anterolateral segments or left or right hepatectomy were placed in French position, 15 to 30-degrees reverse-Trendelenburg. Patients undergoing resection of the posterosuperior segments were placed in left lateral position. Subsequently, the robot was docked over the patient's head or, when the patient was placed in left lateral position, over the patient's right shoulder in case of the da Vinci Si or da Vinci X. The robot was docked from the patient's right side in case of da Vinci Xi. Three or four robotic ports were used and one or two conventional laparoscopic ports were placed for assistance. Intraoperative ultrasound using a drop-in probe (Hitachi Aloka) enabling integrated use with the robotic system was used where appropriate. A pringle manoeuvre was applied when deemed appropriate using a vessel loop or endo bulldog. In all procedures, The EndoWrist ® One™ Vessel Sealer (Extend) (Intuitive Surgical Inc., Sunnyvale, CA, USA) was used for transection of the hepatic parenchyma, usually combined with a bipolar Maryland Forceps (Intuitive Surgical, Sunnyvale, California, USA). Hem-o-lok clips (Teleflex Inc., Morrisville, NC, USA) or laparoscopic staplers (Medtronic, Minneapolis, MN, USA) were used to control the hepatic pedicles and larger branches of the hepatic veins. In most procedures, TachoSil (Takeda Nederland b.v., Takeda, Zurich, Switzerland) was applied to the resection surface. The specimen was extracted through an enlarged trocar incision or, in case of major liver resection, through a Pfannenstiel incision.

Surgical technique - Robotic pancreatoduodenectomy

The technique used for robotic pancreatoduodenectomy was adapted from the technique as previously described by the University of Pittsburgh Medical Center (UPMC). [26] Patients were placed in French position, with the tableside surgeon standing between the patient's legs. Four robotic arms were used. Three additional laparoscopic ports were placed subsequently. Two for assistance and one for the introduction of a liver retractor. The surgical robot was docked over the patient's head. Hereafter, a classic Whipple resection was performed. Reconstruction was carried out through three anastomoses. First, the pancreaticojejunostomy was performed using a modified Blumgart technique. Next, an interrupted end-to-side hepaticojejunostomy was performed using PDS 5-0 sutures. Finally, a stapled gastrojejunostomy was carried out. A surgical drain was placed and the specimen was removed through an enlarged trocar incision.

Results

Between August 1st , 2015 and March 1st , 2019, 77 consecutive robotic liver resections were performed in 74 patients. Three patients underwent robotic liver resection twice. During this time period, 68 consecutive robotic pancreatoduodenectomies were performed as well. These numbers include the first procedures performed, for both liver resection and pancreatoduodenectomy. A global timeline of the initiation of the robotic HPB procedures is provided in Figure 1. Over the past years, the percentage of procedures that were performed robotically gradually increased. (Figure 2)

Implementation scheme

A schematic representation of the different starting points in time of the five HPB surgeons (numbered 1 until 5) is displayed in Figure 3. Prior to the start of the robotic liver surgery program, surgeon 1 and surgeon 2 visited an expert surgeon in robotic liver surgery three times. The first procedures performed were minor resections of the anterolateral segments. Surgeon 1 performed the first robotic liver resections to create continuity in the learning curve. After approximately sixteen procedures, surgeon 2 performed his first robotic liver resection and thereafter the other surgeons started performing robotic liver resection, first as tableside assistant and subsequently behind the console. Over time, indications extended and major liver resections were also performed robotically.

The robotic pancreatoduodenectomy program was preceded by a visit to a US expert center for robotic pancreatoduodenectomy (University of Pittsburgh Medical Center; UPMC) by surgeon 1 and surgeon 3. The same expert surgeon from this center proctored the first two robotic pancreato-duodenectomies on-site. Surgeon 3 performed the first robotic resections; the reconstruction phase was alternated between the different surgeons in an earlier phase of the implementation. All robotic pancreatoduodenectomies were performed by at least two HPB surgeons; switching roles during the procedure, alternating operating behind the console for the resection phase and the reconstruction phase.

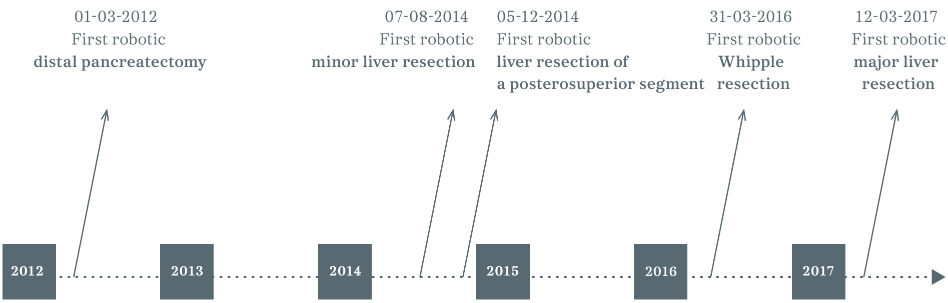

Figure 1. Global timeline of the initiation of robotic HPB procedures

Baseline characteristics

A summary of baseline characteristics of patients undergoing robotic liver resection or robotic pancreatoduodenectomy is provided in Table 1. Most liver resections were performed for colorectal liver metastasis. Most pancreato-duodenectomies were performed for a proven or suspected malignancy.

Surgical parameters and clinical outcomes

A summary of the surgical details of the robotic HPB procedures and the clinical outcomes of the patients undergoing either liver resection or pancreato-duodenectomy is provided in Table 2.

For liver resection, minor resections of the anterolateral segments were most frequently performed. Five procedures (including two major resections, one minor resection of a anterolateral segment and two resections of the postero-superior segments) were converted to a laparotomy, mostly due to the lack of overview during parenchymal transection. Median postoperative hospital stay was four days. One patient died postoperatively due to post-hepatectomy liver failure. This patient underwent right hepatectomy for a hepatocellular carcinoma and developed multiple organ failure during his postoperative course. However, this was most likely a result of the extent of the resection rather than of the robotic approach.

In total, nine (13%) robotic pancreatoduodenectomies were converted to a laparotomy, for several reasons including: failure to progress, severe adhesions and portal/superior mesenteric vein bleeding. In 22 patients (32%) a grade B/C pancreatic fistula occurred, four patients (6%) suffered from a grade B/C post-pancreatectomy hemorrhage. There was no in-hospital or 30-day mortality and median length of hospital stay was 14 days (IQR: 9-22).

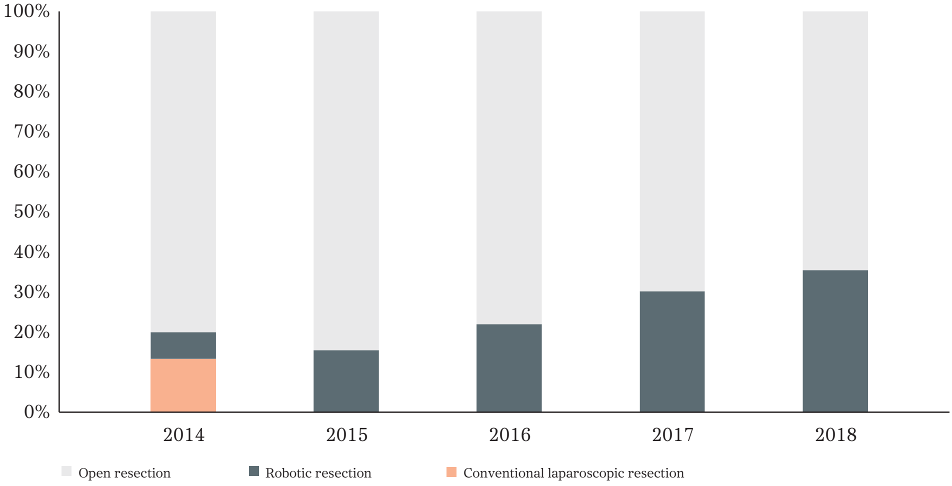

Figure 2. Percentage of all liver resections performed robotically, per year, RAKU location: UMC Utrecht Cancer Center

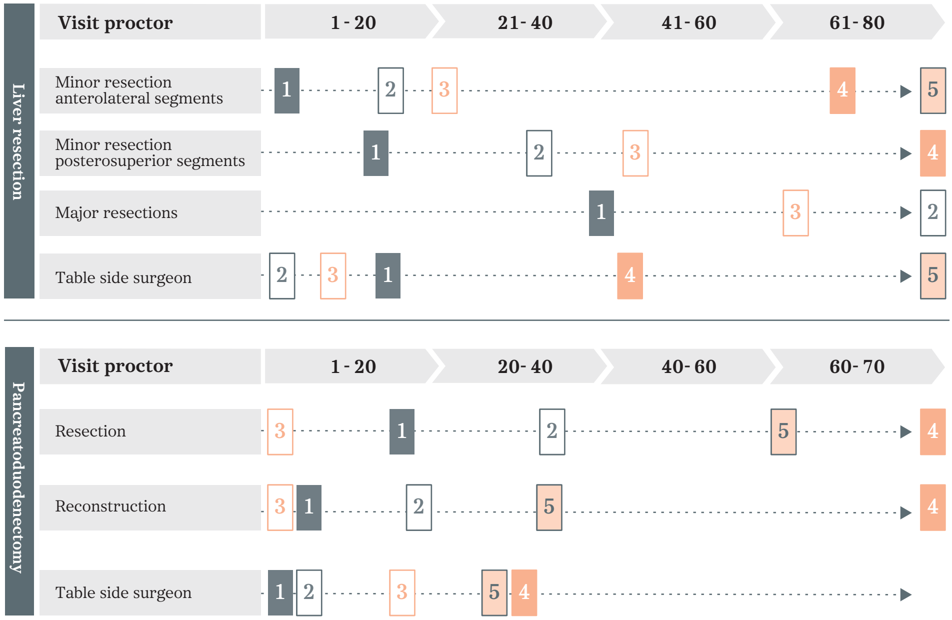

Figure 3. Stepwise implementation of five surgeons in robotic pancreatoduodenectomy and liver resection

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Table 1. Baseline characteristics

Characteristic	n (%) ^
Pancreatoduodenectomy	68
Age, mean (SD), years	65 (14)
Sex, male	32 (47)
BMI, mean (SD), kg/m^2	26 (5)
ASA score [1]	
ASA 1	5 (7)
ASA 2	41 (60)
ASA 3	21 (31)
Previous abdominal surgery	20 (29)
Indication for resection	
Proven or suspected malignancy	45 (66)
Premalignant cystic lesion	13 (19)
Neuro-endocrine tumor	5 (7)
Benign	5 (7)
Liver resections	77
Age, mean (SD), years	60 (15)
Sex, male	38 (49)
BMI, mean (SD), kg/m^2	27 (5)
ASA score [2]	
ASA 1	4 (5)
ASA 2	52 (68)
ASA 3	18 (23)
Previous abdominal surgery	50 (65)
Indication for resection	
CRLM	35 (46)
Metastasis, other	9 (12)
HCC	17 (22)
Benign	10 (13)
Cholangiocarcinoma	5 (7)
Other	1 (1)

Abbreviations: SD: standard deviation; BMI: body mass index; ASA: American Society of Anesthesiologists; CRLM: colorectal liver metastasis; HCC: hepatocellular carcinoma. Legend: [1] one missing; [2] three missings; ^ reported as 'n (%)', unless stated otherwise.

Table 2. Surgical details and clinical outcomes

Characteristic	n (%) ^
Pancreatoduodenectomy	68
Operative time, mean (SD), minutes*, [1]	420 (67)
Estimated blood loss, median (IQR), mL[2]	325 (193-725)
Conversion	9 (13)
PPH ~	4 (6)
POPF ~	22 (32)
DGE ~	15 (22)
Bile leakage $	8 (12)
Unplanned ICU admission	5 (7)
Length of stay, median (IQR), days	14 (9-22)
In-hospital or 30-day mortality	0 (0)
Liver resection	77
Minor resection solely including anterolateral segments	36 (47)
Minor resection including posterosuperior segments	30 (39)
Major resection (right and left hepatectomy)	11 (14)
Operative time, mean (SD), minutes*,[3]	160 (78)
Estimated blood loss, median (IQR), mL[4]	125 (33-300)
Conversion	5 (7)
Bile leakage $	3 (4)
Unplanned ICU admissions	3 (4)
Length of stay, median (IQR), days	4 (3-6)
In-hospital or 30-day mortality	1 (1)

Abbreviations: SD: standard deviation; IQR: interquartile range; PPH: postpancreatectomy hemorrhage; POPF: postoperative pancreatic fistula; DGE: delayed gastric emptying; ICU: intensive care unit. Legend: *Corrected for additional procedures; ~ ISGPS grade B/C;$ ISGLS grade B/C. ^ reported as 'n', unless stated otherwise; [1] one missing; [2] two missing; [3] one missing; [4] one missing.

Operative times

To visually estimate the effect of the addition of different surgeons in the learning process and to evaluate if this approach affects operative time, the operative times for each of the procedures (for both liver resection and pancreatoduodenectomy) are displayed in Figure 4, chronologically pooled in groups of 10 resections.

Discussion

In this study we describe a stepwise implementation and expansion scheme of robotic liver resection and pancreatoduodenectomy in a high volume practice in the Netherlands. Second, we provide a summary of the clinical outcomes and surgical details of all robotic liver resections and robotic pancreatoduodenectomies performed within this program. Our study demonstrates that stepwise expansion of robotic HPB surgery within one unit is feasible and associated with good clinical outcomes. Despite introducing new surgeons to robotic HPB surgery, operative times, as an indicator for a learning curve, remained stable over time.

Over the past years, robotic surgery has become increasingly important as an alternative to conventional laparoscopy, in HPB surgery as well. [9, 10] Consensus meetings on the initiation of a robotic program have resulted in several papers on this subject and there is an increased interest for robotic training during residency and fellowship. [12-16, 27] The further growth of a robotic HPB program run by a team of surgeons, however, has not yet been addressed, although this forms an important step after the initiation of one's program. In our program, surgeons with different levels of experience were introduced to the new technique in a stepwise fashion. Of note, the two surgeons who played the main role at the initiation phase both had extensive experience in open liver resection and open pancreatoduodenectomy. Moreover, there was already extensive experience in our center with robotic surgery in other surgical specialties (including thyroidectomies and esophagectomies). Overall, this approach resulted in a stable program, not dependent on a single surgeon.

Several papers on learning curves in robotic liver resection and robotic pancreatoduodenectomy have been published, aimed to identify inflexion points in a learning process, mostly using cumulative sum (CUSUM) analyses. [28, 29] In most of these papers, operative time is used (among others) as a parameter indicating the learning curve. In our study, we did not perform CUSUM analysis, since this was not the aim of the paper. However, we did provide operative times, chronologically, to visually identify trends over time. For robotic liver resection, operative times remained stable over time. The lack of a decrease in the operative times is most likely a result of extending indications and the increase in major liver resections that have been performed. For robotic pancreatoduodenectomy, operative times remained relatively stable over time

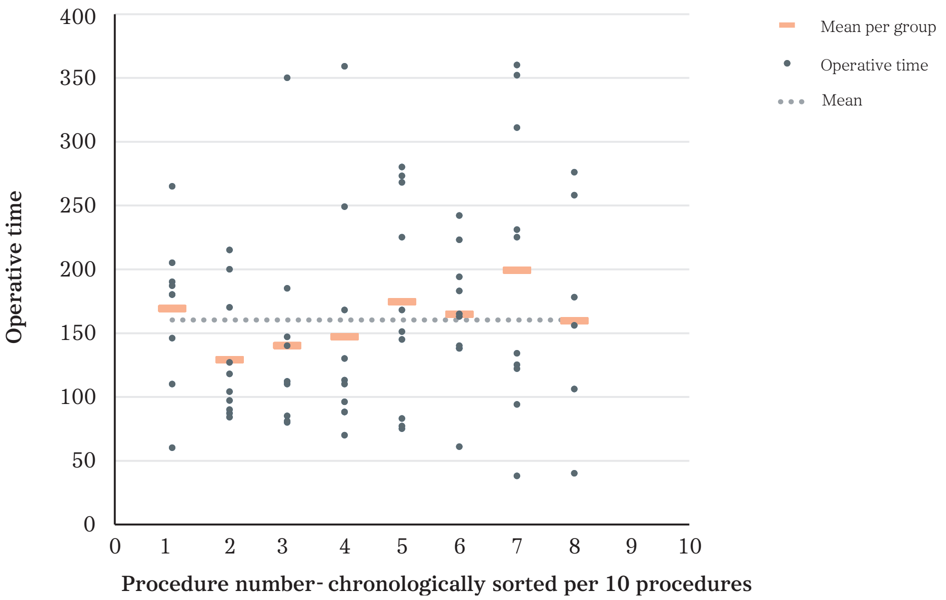

Figure 4.1. Operative times robotic liver resections

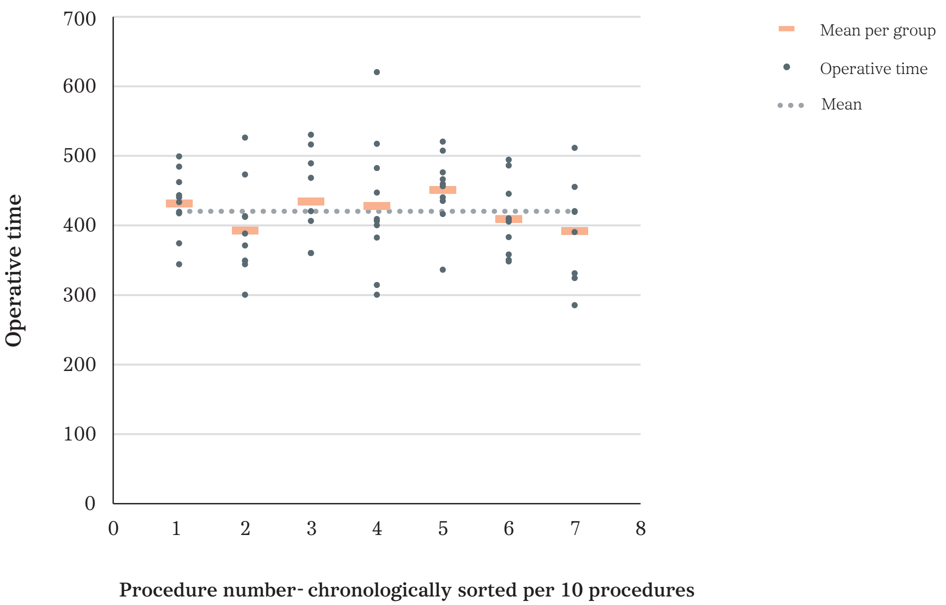

Figure 4.2. Operative times robotic pancreatoduodenectomies

and the mean duration of surgery was 420 minutes. In a study from University of Pittsburgh Medical Center, an expert center in robotic pancreatoduodenectomy, a mean operative time of 420 minutes was achieved after approximately 80 procedures. [30] This strengthens the hypothesis that implementing and expanding robotic pancreatoduodenectomy according to a stepwise scheme leads to a plateau in operative times on relatively short notice.

This study has several shortcomings which should be taken into account. First, although the described manner of expanding robotic HPB has proven to be feasible in our center, implementing our exact scheme in different centers is not the aim of this report. However, we do believe the described manner can provide a tool for surgeons who initiate a robotic HPB program and want to expand their practice. Second, since the program is run by five different surgeons, this way of setting up the program potentially slows down one's individual learning curve. On the contrary, the surgeons go through the learning process as a team. Since the surgeries can be performed by different members of the team, this results in a stable program, not dependent of a single surgeon. Third, clinical outcomes as presented in this study might be influenced by the learning curve of the team, since, for both liver resection and pancreatoduodenectomy, the initial procedures were included as well. Thus, potentially these results and the operative times might further improve over time.

Conclusion

In conclusion, stepwise implementation and expansion of robotic HPB surgery within one unit is feasible and associated with good clinical outcomes. Despite introducing new surgeons to the technique, operative times, an indicator of the learning process, remained stable over time.

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Chapter 10

Video Chapter Robotic Pancreatoduodenectomy for a Solid Pseudopapillary Tumor in a Ten-Year-Old Child

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Abstract

Background

Pancreatoduodenectomy (Whipple resection) in children is feasible though rarely indicated. In several pediatric malignancies of the pancreas, however, it may be the only curative strategy. [1] With the emergence of robotic pancreatoduodenectomy as at least a clinically equivalent alternative to open surgery, [2] it remains to be determined whether the pediatric population may potentially benefit from this minimally invasive procedure. Here we present, for the first time, a video of set-up and surgical technique of robotic pancreatoduodenectomy in a child.

Methods

A 10-year-old girl presented with complaints of fullness and abdominal pain in the upper quadrants. Investigations including a diffusion-weighted, pancreatic MR scan suggested the diagnosis of solid pseudopapillary tumor (Frantz's tumor). The patient was considered for robotic pancreatoduodenectomy.

Results

After anesthesia, the patient was placed supine on a split-leg table. Trocar placement was adjusted to accommodate the child's length and body weight, according to pre-operatively calculated positions that would allow for maximum working space and minimize inadvertent collision between the robotic arms. The da Vinci Si surgical robot was positioned in-line towards the surgical target and all four robotic arms were docked, while two additional laparoscopic ports were placed for tableside assistance. After standard pancreatoduodenectomy, a conventional loop reconstruction was performed including an end-to-side pancreaticojejunostomy with duct-to-mucosa technique and stapled side-to-side gastrojejunostomy. We suggest that in this patient group, pylorus preserving pancreatoduodenectomy with end-to-side duodenojejunostomy may be a suitable alternative. Postoperative recovery was complicated by delayed gastric emptying but otherwise unremarkable. Hospital length of stay was 12 days. Final pathology demonstrated a solid pseudopapillary tumor with negative surgical margins.

Conclusion

This case illustrates the feasibility of robotic pancreatoduodenectomy in children. Essential elements of this procedure are a well-running robotic pancreatic surgery program as well as careful preoperative port placement planning.

Video

QR code to video

Link to video

https://www.sciencedirect.com/science/article/pii/S0960740418301026?via%3Dihub

or

https://player.vimeo.com/external/247413283.hd.mp4?s=468a968feb6f854a4ea6a4f528616c0e2a504846&profile_id=174

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Chapter 11

The First 100 Robotic Pancreatoduodenectomies in the Netherlands

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Adapted from

Robotgeassisteerde Whipple-Operatie:
Resultaten van de Eerste 100 Ingrepen in Nederland

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Abstract

Objective

Reporting the results of robotic Whipple procedures in the Netherlands. These results were compared with those of open Whipple procedures on the basis of recent large case series of patients.

Design

Case series of patients and systematic literature review.

Methods

We carried out a *post hoc* analysis of prospectively collected data on the first 100 consecutive patients who underwent a robotic Whipple procedure in the period from March 2016 until March 2018 at the Erasmus MC, the Maasstad hospital or the Regional Academic Cancer Center Utrecht. We were mainly interested in the surgical characteristics and postoperative outcomes. We compared our results with those of case series of patients with more than 500 open Whipple procedures carried out in a single hospital, published in the last 5 years.

Results

There were one or more major complications in 22 patients (22%) and 2 patients (2%) developed multiple organ failure. A total of 7 patients (7%) underwent a reoperation. There was no postoperative mortality. In 14 case series (n = 12,708), complications occurred in 38% of the patients and 7% of all patients underwent a reoperation. Mean mortality rate was 3%.

Conclusion

Our findings show that robotic Whipple procedures can be carried out safely in the Netherlands. The number of complications and mortality rates are comparable with results of large case series of patients who underwent open Whipple procedures in a center of expertise.


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ROBOTGEASSISTEERDE WHIPPLE-OPERATIE
MEDICATIEGEBRUIK IN DE ZWANGERSCHAP
ANTISTOLLING COUPEREN MET ANDEXANET?
NATTE MACULADEGENERATIE BIJ OUDEREN
ONLINE TOETS

Introduction

The Whipple procedure - also called 'pancreatoduodenectomy' - is a complex surgical procedure during which the pancreatic head, the duodenum, the distal bile ducts and the gallbladder are removed. After resection, the gastrointestinal continuity is restored by construction of three anastomoses: the pancreaticojejunostomy, the hepaticojejunostomy and the gastrojejunostomy. (Figure 1) The Whipple procedure is considered a complex procedure with significant morbidity and mortality rates. Despite that, a Whipple resection is the only potentially curative treatment for patients with pancreatic cancer in the head of the pancreas, distal cholangiocarcinoma, ampullary carcinoma and duodenal cancer. Moreover, clinical outcomes of Whipple resections have dramatically improved over the last decade due to centralization of care and improved perioperative care. This is, among others, the reason that the number of Whipple resections performed in the Netherlands is increasing, also for patients with premalignant cystic lesions in the pancreas. [1]

Almost all frequently performed abdominal surgeries, such as cholecystectomy or appendectomy, are performed through laparoscopic surgery in the Netherlands. In conventional laparoscopic surgery, the surgeon inserts prolonged instruments and a camera in the peritoneal cavity through several small (5-15 mm) incisions. The surgeon stands next to the operating table and the operative field is visualized on a (mostly) two-dimensional monitor. However, due to the complexity of the procedure, the Whipple procedure is usually performed through open surgery making a 30 cm incision and thereby splitting the abdominal wall musculature. In the Netherlands, laparoscopic Whipple procedures are no longer performed due to safety concerns of the laparoscopic approach. Recently, a Dutch randomized, multicenter trial, comparing laparoscopic Whipple procedures with open Whipple procedures, was terminated at interim analysis due to increased mortality in the laparoscopic group. [2]

Robotic Whipple procedures

Robotic surgery provides an alternative to conventional laparoscopic Whipple procedures. Long instruments are inserted in the abdominal cavity through small incisions and connected to the surgical robot. This technique differs from conventional laparoscopy in three important areas: (1) instruments are

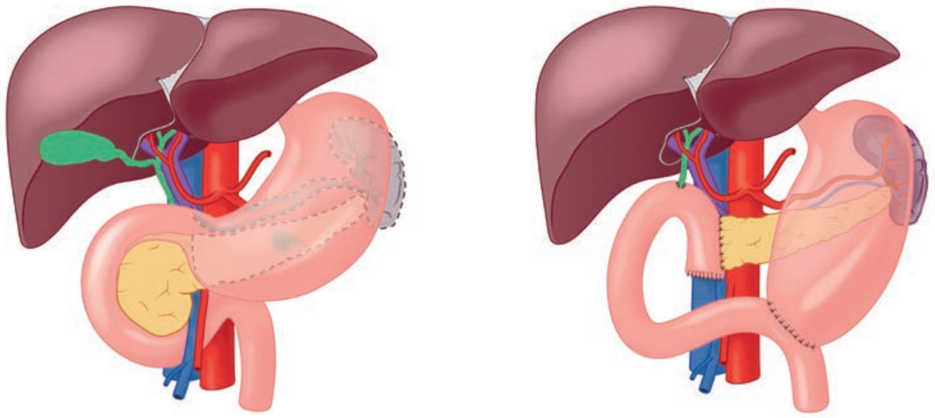

Figure 1. Schematic representation of a pancreatoduodenectomy (left: resected structures, right: after reconstruction) The dashed lines indicate the structures that will be resected. Gastrointestinal continuity is restored by the construction of three anastomoses: the pancreaticojejunostomy, hepaticojejunostomy, and the gastrojejunostomy

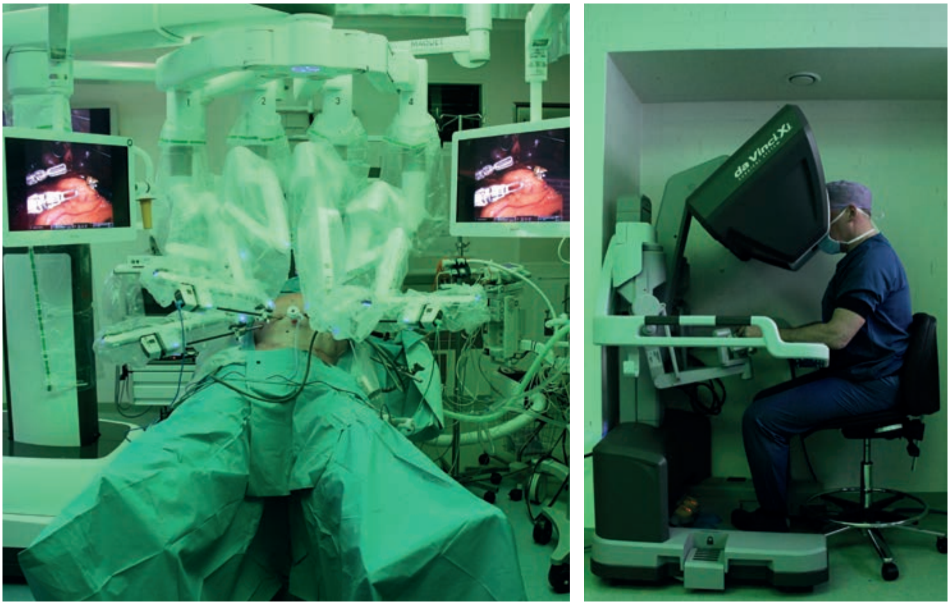

Figure 2. The surgical robot is connected to the prolonged instruments (picture on the left); the surgeon operates from behind te console (picture on the right)

wristed with more freedom of motion than a human hand; (2) the surgeon operates from behind a console. In the console, the view of the surgical field is ten times magnified and displayed three-dimensionally. Moreover, operating from behind the console offers ergonomic benefits for the surgeon; (Figure 2) (3) tremors are filtered and movements are scaled (standard 1:3).

With the use of the surgical robot, one can operate through minimally invasive surgery without compromising surgical dexterity as experienced in open surgery. An important difference between the Whipple procedure and other minimally invasive conventional laparoscopic procedures is the technical complexity of the construction of the three anastomoses of the Whipple procedure. Especially the pancreaticojejunostomy can be highly complex, for the pancreatic duct that needs to be anastomosed can be only as wide as 1 mm. Benefits of a minimally invasive approach to the Whipple procedure are less blood loss, fewer blood transfusions, enhanced recovery after surgery, shorter time to the administration of adjuvant chemotherapy and fewer long-term complications such as major abdominal hernias. [3-7]

In this study, we describe the outcomes of the first 100 robotic Whipple procedures in the Netherlands, performed since 2016 in three different, high-volume Dutch hospitals. We have compared these results to results of recent, large patient series on open Whipple procedures. Aim of this study was to determine whether robotic Whipple procedures can be performed safely after structured implementation in Dutch hospitals.

Methods

Design

We performed a *post hoc* analysis of prospectively collected data on the first 100, consecutive patients who underwent a robotic Whipple procedure between March 2016 and March 2018 in Erasmus MC, the Maasstad Hospital and Regional Academic Cancer Center Utrecht (RACU; locations: UMC Utrecht and St. Antonius Hospital).

Prior to the start of the first robotic Whipple procedures, the surgeons involved attended a formal training from Intuitive Surgical (manufacturer of the surgical robot that is employed in the Netherlands), in the context of a structured Dutch implementation program for this new surgical technique. Subsequently, they did case observations in foreign centers of expertise in robotic Whipple procedures. All the involved surgeons already had experience with less complex robotic procedures and extensive experience with open Whipple procedures. Furthermore, they had access to hours of video material of robotic Whipple procedures performed by expert surgeons. Finally, they practiced construction of the anastomoses on silicon organs, similar to human organs.

The first procedures in the Netherlands were proctored by an experienced surgeon from a foreign expertise center. Due to the complexity and length of the procedure, all procedures were performed by at least two experienced hepato-pancreato-biliary surgeons. In all three hospitals there was extensive experience with robotic oncologic surgery, in different fields. The premise of this meticulous preparation was that it would be unacceptable for patients to have a higher risk of complications because of the introduction of a new surgical technique.

Patients were selected for a robotic approach in a multidisciplinary meeting. This study was conducted according to the Strengthening The Reporting of Observational Studies in Epidemiology (STROBE) guidelines. [8]

Data collection

Patient characteristics, operative details and postoperative outcomes were collected from three databases and analyzed *post hoc*. Patient characteristics consisted of: sex, age, BMI, ASA score, previous abdominal surgery and indication for resection. Operative details collected were: operative time, blood loss and conversion to laparotomy. The postoperative outcomes consisted of: histopathologic diagnosis, tumor size, margin status, postoperative complications, surgical interventions, ICU admissions, organ failure, length of stay, readmissions and mortality.

Definitions

Complications such as postoperative leakage of the pancreaticojejunostomy (pancreatic fistula), postpancreatectomy hemorrhage, delayed gastric emptying and postoperative chyle leakage are defined and scored using the International Study Group of Pancreatic Surgery (ISGPS) classifications. [9-12]

Bile leakage was defined and scored using the International Study Group of Liver Surgery (ISGLS) classification. [13] Conversion was defined as any other laparotomy made during the robotic Whipple procedure than for specimen extraction. New-onset organ failure was defined as follows: 1) respiratory insufficiency: a PaO2 < 60 mm Hg despite FiO2 of 0,3 or the need for mechanical ventilation; 2) circulatory failure: a systolic blood pressure below 90 mm Hg despite accurate fluid resuscitation or the need to start inotropes or vasopressors; 3) renal failure: a serum creatinine over 177 µmol/L after fluid resuscitation or the need to start CVVH or hemodialysis. [14] The resection was considered oncologically radical if there were no tumor cells in the transection plane or within 1 mm of the transection plane (R0). The resection was considered oncologically irradical if there were tumor cells in the transection plane or within 1 mm of the transection plane. [15] Postoperative complications were scored during index admission. A 'major complication' was defined as the occurrence of one or more of the following: ISGPS grade B/C postpancreatectomy hemorrhage, ISGPS grade B/C pancreatic fistula, multiple or single organ failure or death. If a patient was readmitted within ten days after discharge, this second admission was still considered 'index admission'.

Systematic literature review

To put our results into perspective and to determine the safety of the robotic Whipple procedure, we have compared the outcomes of our study to large, recent patient series on open Whipple procedures, published the last five years. A systematic search was performed on August 15th 2018 in PubMed using a predefined search strategy and using the following search query:

((pancreatoduodenectom*[Title/Abstract]) OR (pancreaticoduodenectom*[Title/Abstract]) OR (Whipple*[Title/Abstract])) AND ((mortality[Title/Abstract] OR death[Title/Abstract]) AND (morbidity[Title/Abstract] OR complication*[Title/Abstract])) AND ("2013/08/15"[Date -Publication] : "2018/08/15"[Date - Publication]).

We included patient series reporting outcomes of more than 500 open Whipple procedures, performed in a single center. We excluded studies in which no separate outcomes were given for the minimally invasive procedures and studies in which there were no data provided on any of the following parameters: reoperations, mortality, postoperative complications, postoperative

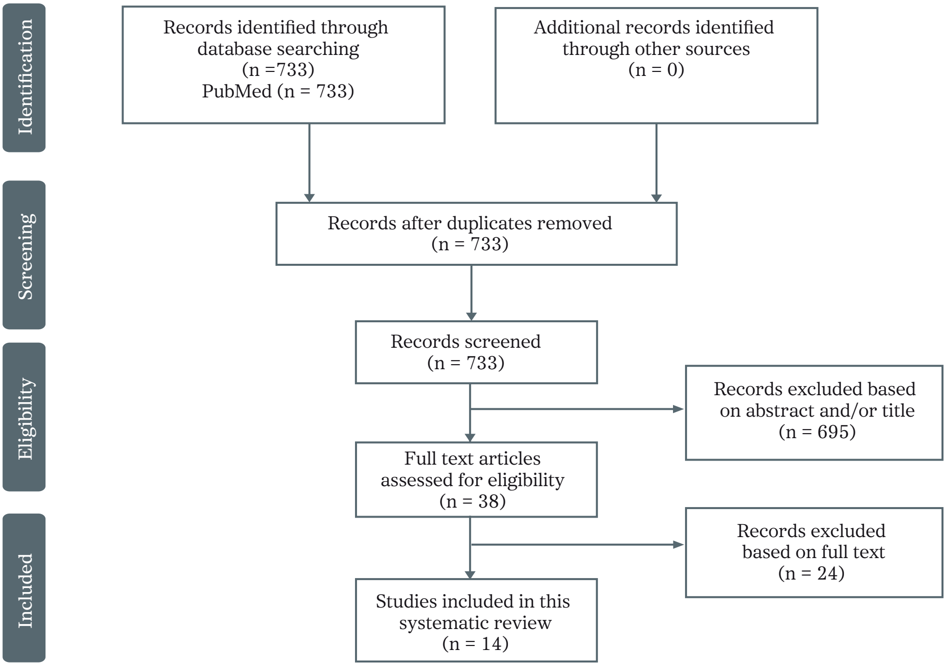

Figure 3. Flow diagram of the included studies.

pancreatic fistula or postpancreatectomy hemorrhages. If there were multiple studies from the same research group, we solely included the study in which most of the abovementioned parameters were reported or - if the number of reported parameters was the same in multiple studies from the same center - the study reporting the outcomes of the largest number of patients. The flow diagram of the included studies in provided in Figure 3. 11

Statistical analysis

Data with a normal distribution were reported as mean and standard deviation (SD). Data with a skewed distribution were reported as median and interquartile range (IQR).

Results

Patient characteristics

Patient characteristics of the first 100 patients who underwent a robotic Whipple procedure are provided in Table 1. From the start of the robotic Whipple program in each center, there were also 150 open Whipple procedures performed in the three centers. The most important reasons to refrain patients from a robotic Whipple procedure were as follows: vascular involvement of the tumor, one or more extensive abdominal surgeries in their past medical history, severe pancreatitis, potentially causing extensive intra-abdominal adhesions. Mean age was 66 years (SD: 11) en 57% was male. In 78 patients (78%) a suspected or proven malignancy was the indication for resection.

Surgical details

Surgical details are provided in Table 2. In 8 patients (8%) the robotic procedure was converted to a laparotomy, for several reasons. In four patients a bleeding from the portal vein or superior mesenteric vein occurred that could not be controlled robotically, in three patients a lack of progress during the resection phase of the surgery was reason for conversion and one patient had severe intra-abdominal adhesions following previous abdominal surgery. A total of seven patients (7%) had to undergo a reoperation for (the suspicion of) a postoperative bleeding (n= 3), revision of the gastrojejunostomy (n= 2), leakage of the gastrojejunostomy (n= 1) and repair of a small trocar hernia (n=1).

Postoperative outcomes

Postoperative outcomes are displayed in Table 2 as well. In 22 patients (22%) one or more major complications occurred. Two patients (2%) developed multiple organ failure. None of the patients died during index admission. There were two patients who died within 90 days after surgery. Both patients had an early recurrence of a pancreatic adenocarcinoma and died of disease progression rather than as a result of the surgery.

Comparison with the literature

The results of the systematic literature review are provided in Table 3. In total, 14 patient series (n =12,708) from high-volume expert centers met the inclusion criteria. The mean mortality after open Whipple resection was 3% and the mean morbidity was 38%. In 15% of the patients a postoperative pancreatic fistula occurred and in 7% of the patients a postpancreatectomy hemorrhage occurred. In total, 7% of the patients in this pooled analysis had to undergo a reoperation. Results from this meta-analysis are comparable to the results of our first 100 robotic Whipple procedures.

Table 1. Patient characteristics

Characteristic	n (%) ^
Center	
RAKU	36 (36)
Erasmus MC	34 (34)
Maasstad Hospital	30 (30)
Year of surgery	
2016	9 (9)
2017	74 (74)
2018	17 (17)
Age, mean (SD), years	66 (11)
Sex, male	57 (57)
BMI, mean (SD), kg/m^2	26 (5)
ASA score	
ASA 1	10 (10)
ASA 2	62 (63)
ASA 3	27 (27)
Previous abdominal surgery	31 (31)
Indication for resection	
Suspected or proven malignancy	78 (78)
Premalignant cystic lesion	11 (11)
Neuroendocrine tumor	5 (5)
Benign pathology	6 (6)

Abbreviations: RAKU: Regional Academic Cancer Center Utrecht; SD: standard deviation; BMI: body mass index; ASA: American Society of Anesthesiologists. Legend: ^ reported as 'n (%)', unless stated otherwise.

Table 2. Surgical details and postoperative outcomes

Characteristic	n (%) ˆ
Surgical details	
Operating time, mean (SD), min.	423 (119)
Blood loss, median (IQR), mL	250 (150-700)
Conversion to laparotomy	8 (8)
Histopathological outcomes	
Definitive diagnosis	
Pancreatic adenocarcinoma	45 (45)
Distal cholangiocarcinoma	13 (13)
Duodenal carcinoma	4 (4)
Ampullary carcinoma	9 (9)
Intraductal papillary mucinous neoplasm (IPMN)	7 (7)
Neuroendocrine tumor	6 (6)
Other, benign	13 (13)
Other, malignant	3 (3)
Radical (R0) resection*	51 (64)
Pathology, malignant	80 (80)
Tumor size, mean (SD), mm	27 (14)
Lymph nodes total, mean (SD)	13 (6)
Tumor positive lymph nodes , median (IQR)	0 (0-3)
Postoperative outcomes	
Patients with one or more severe complications	22 (22)
Post-pancreatectomy hemorrhage (grade b/c)#	9 (9)
Delayed gastric emptying (grade b/c)#	26 (26)
Pancreatic fistula (grade b/c)#	19 (19)
Bile leakage (grade b/c)˜	9 (9)
Patients with single organ failure	2 (2)
Patients with multiple organ failure	2 (2)
Unplanned intensive care admissions	12 (12)
Death	0 (0)
Surgical intervention	
Relaparotomy	7 (7)
Radiological intervention	
Percutaneous drainage	21 (21)

Abbreviations: SD: standard deviation, IQR: interquartile range. Legend: * solely reported for malignancies (n=80), # ISGPS classification, ˜ ISGLS classification. Legend: ˆ reported as ‘n (%)’, unless stated otherwise.

Table 3. Comparison with literature

Authors	Year	Country	Number of patients	Mortality	Reoperations	POPF	PPH	Morbidity
Cameron et al.	2015	USA	2000	1,6 % [e]	3,5 %	15,0 % [i]	1,6 % [j]	45,0 % [g]
De Pastena et al.	2018	IT	1500	1,9 % [a]	8,7 %	20,7 % [b]	13,4 % [c]	21,8 % [d]
El Nakeeb et al.	2017	EG	742	4,7 % [e]	7,8 %	13,6 % [c]	4,4 % [i]	33,8 % [g]
Epelboym et al.	2014	USA	506	4,2 % [h]	8,9 %	5,1 % [c]	NR	49,4 % [g]
Eshuis et al.	2014	NL	1036	2,0 % [e]	9,7 %	15,1 % [b]	6,5 % [f]	59,6 % [g]
Feng et al.	2014	CN	840	3,3 % [e]	NR	19,9 % [c]	8,7 % [c]	36,6 % [g]
Fong et al.	2014	USA	1173	1,8 % [a]	2,5 %	13,6 % [i]	3,6 % [i]	32,6 % [g]
Fu et al.	2015	CN	532	4,3 % [h]	4,5 %	10,2 % [b]	11,3 % [c]	22,4 % [d]
Jester et al.	2017	USA	924	4,3 % [a]	6,4 %	23,5 % [c]	NR	28,1 % [k]
Kulemann et al.	2017	DE	553	1,9 % [e]	12,1 %	15,2 % [b]	9,8 % [c]	59,5 % [g]
Nagle et al.	2017	USA	1090	3,3 % [a]	NR	17,2 % [c]	NR	NR
Pugalenthi et al.	2016	USA	596	3,7 % [a]	NR	4,2 % [i]	1,8 % [i]	51,0 % [g]
Seppanen et al.	2017	FI	581	2,1 % [e]	6,9 %	7,0 % [b]	NR	NR
Temple et al.	2014	CA	635	1,6 % [l]	NR	12,0 % [c]	7,7 % [c]	17,3 % [d]
Weighted means				2,7 %	6,5 %	15,0 %	6,5 %	37,7 %

Abbreviations: NR: not reported; POPF: postoperative pancreatic fistula; PPH: postpancreatectomy hemorrhage. Legend: [a] 90-day mortality; [b] reported as clinically relevant (ISGPS grade B/C); [c] ISGPS grade A/B/C; [d] major complications (Clavien-Dindo ≥ grade III); [e] in-hospital mortality; [f] reported as ISGPS grade B/C; [g] total morbidity; [h] during index admission or within 30 days after resection; [i] no definition or grading; [j] solely late bleedings reported; [k] 'major morbidity' using own definition; [l] during index admission or within 90 days after resection.

Discussion

Our study describing the first 100 consecutive patients who underwent a robotic Whipple procedure in Erasmus MC, the Maasstad Hospital and RACU, shows that a minimally invasive Whipple procedure can be performed safely through robotic surgery and that het number of patients who suffered from postoperative complications was limited. Our results are comparable to the outcomes of large, recent series on patients who underwent open Whipple procedures in expert centers.

Benefits of a minimally invasive Whipple procedure

Systematic literature reviews and meta-analyses demonstrate several potential patient benefits of a minimally invasive approach to the Whipple procedure such as less blood loss, fewer major complications and an enhanced recovery after surgery. [4-6] Potentially more patients can undergo adjuvant chemotherapy in this way. [7] There are, however, to date no randomized studies comparing robotic Whipple procedures to their open counterpart. [16, 17] There are also several long-term benefits of a minimally-invasive approach to a Whipple procedure such as fewer major abdominal hernias in absence of a large incision and fewer adhesions. These advantages are namely beneficial for the growing number of patients undergoing Whipple resection for a premalignant, cystic lesion. These patients are relatively young in general and have - compared to patients with a pancreatic adenocarcinoma - a long life expectancy, which means that these long-term complications should be taken into account.

Safety

In the Netherlands, conventional laparoscopic Whipple procedures are no longer performed due to safety concerns of this technique. A case series of 114 patients undergoing laparoscopic Whipple resection from four Dutch hospitals and two randomized controlled trials from India and Spain demonstrated adequate results initially. However, recently, a randomized controlled Dutch trial was terminated at interim analysis, since the mortality in the laparoscopic group was higher than in the group of patients undergoing an open Whipple resection. (10% vs. 2%; $p = 0.2$). [2] Possible explanations for this unfavorable outcome are the small number of patients that was operated on in the participating hospitals and the long learning curve of laparoscopic Whipple procedures. An increasing number of studies on robotic Whipple procedures from American expertise centers is being published. [21, 22] In general, a trend is observed where the number of laparoscopic procedures is decreasing and the number of robotic procedures is increasing. [23] In our study there were 22 patients with a severe complication. These were, however, mainly patients with a pancreatic fistula who underwent simple, radiological percutaneous drainage. Solely two patients developed multiple organ failure and none of the patients died.

Limitations

Our study was limited by several factors. First, we analyzed the first procedures performed in the three hospitals. There is a learning curve, which potentially affects the current results. A study from an American expertise center where robotic Whipple procedures have been performed for a long time, demonstrated the learning curve for robotic Whipple procedures. [24] Several indicators for a learning curve such as operating time and incidence of pancreatic fistula, decreased in this study after 80 and 40 procedures, respectively. In our results we could not find any proof of a learning curve. This might be explained by the relatively small number of patients in our study, the intensive proctoring, or by the fact that there were at least two experienced surgeons in the operating room during each procedure. It could well be that results will improve over time if more experience is gained with robotic Whipple procedures.

Second, we selected patients for a robotic Whipple procedure. Among others, patients with tumors with vascular contact, or a medical history of severe pancreatitis were excluded. However, once more experience is gained, these patients could also undergo a Whipple procedure using the surgical robot. [25]

Third, we compared our results indirectly to results of single center patient series from expert centers. Such a comparison is inferior to a direct comparison, such as carried out in a randomized controlled trial, namely due to the heterogeneity in the studies we have included in the meta-analysis. Moreover, our results come from procedures in selected patients, whereas the results in the meta-analysis cover all patients. However, since all of the included series covered the outcomes of over 500 procedures, the meta-analysis does provide a true reflection of the outcomes of patients undergoing a Whipple procedure.

Conclusion

Our results show that minimally invasive Whipple procedures can be performed safely in the Netherlands using the surgical robot. The number of complications and the mortality in our study are comparable to the outcomes of large patient series from expertise centers, describing the results of open Whipple procedures.

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Chapter 12

Oncologic Outcomes after Robot-Assisted versus Laparoscopic Distal Pancreatectomy:

Analysis of the National Cancer Database

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Abstract

Background

How the oncologic outcomes after robotic distal pancreatectomy (RDP) compare to those after laparoscopic distal pancreatectomy (LDP) remains unknown.

Methods

Using the National Cancer Database (NCDB), we analyzed all patients undergoing LDP or RDP for resectable pancreatic adenocarcinoma over a 4-year period (2010-2013).

Results

Of the 704 eligible patients, 605 (86%) underwent LDP and 99 (14%) underwent RDP. The median follow-up for patients was 25 months. There were no differences in the two groups with respect to sociodemographic, clinicopathologic, or treatment characteristics. On comparing LDP versus RDP, there was no difference in the margin-positive rate (15% vs 16%; $p = 0.84$); lymph nodes examined (12 vs. 11; $p = 0.67$); overall survival (hazard ratio: 1.1 (95% confidence interval 0.7 to 1.7); 28 vs. 25 months; $p = 0.71$); hospital stay (6 vs. 5 days; $p = 0.14$); time to chemotherapy (50 vs. 52 days; $p = 0.65$); 30-day readmission (9.4% vs. 9.1%; $p = 0.92$); and mortality (1% vs. 0%; $p = 0.28$). Patients undergoing LDP had a significantly higher conversion rate to open or minimally invasive pancreatic cancer resections compared with RDP (27% vs. 10%; $p < 0.001$).

Conclusion

The early national experience with RDP demonstrates similar oncologic outcomes to LDP, with a significantly lower conversion rate.

Introduction

Robotic surgery for pancreatic cancer is coming of age. Several institutional series have demonstrated that by appropriate patient selection, a team of highly skilled pancreatic surgeons can safely perform a robotic distal pancreatectomy (RDP) with sound oncologic principles. [1-4] Minimally invasive distal pancreatectomy is increasingly favored in specialty centers because it results in decreased pain, a shorter length of stay, and fewer wound-related complications. [5-7] Recently, we found that the short-term and long-term oncologic outcomes for open and laparoscopic distal pancreatectomy (LDP) for pancreatic cancer are comparable. [8]

The robotic platform enables surgeons to overcome some of the technical limitations of conventional laparoscopy. It allows for increased dexterity and depth perception with improved ergonomics. Potentially, the improved precision in surgical dexterity provides several advantages when performing distal pancreatectomy, such as higher spleen preservation rates and less frequent rates of conversion to open resection. [2, 9] Moreover, the precise dissection and enhanced visualization may confer oncologic benefits, such as increased R0 resections and increased number of lymph nodes harvested. [2]

Despite these benefits, the significant cost of robotic instrumentation combined with longer operative time makes it difficult to justify the use of the robotic platform in the current healthcare environment as an alternative to the less resource-intensive laparoscopic approach. [10, 11] However, the cost of RDP is likely to decline in the near future due to the anticipated competition from alternative robotic platforms. As the cost of RDP decreases, the comparative effectiveness of the modalities will become increasingly important. Even though several institutional series have demonstrated the safety of RDP, it is not known whether these findings are generalizable. [1, 2, 4] Furthermore, studies comparing oncologic outcomes between RDP and LDP on a national level are sparse. Therefore, the primary aim of this study was to perform a national comparison of short- and long-term oncologic outcomes of patients undergoing RDP versus LDP for pancreatic cancer in a hospital-based cohort.

Methods

The National Cancer Database (NCDB), jointly sponsored by the Commission on Cancer (CoC) of the American College of Surgeons and the American Cancer Society, is a nationwide oncology outcomes database based on more than 1400 Commission-accredited cancer programs, covering approximately 70% of new cancer cases in the United States. [12] Since the data are publicly available upon request, the study was exempt from institutional review board approval.

Patient selection

Patients diagnosed with pancreatic adenocarcinoma in the body or tail of the pancreas from 2010 to 2013 were identified using International Classification of Diseases for Oncology primary site codes (C25.1 and C25.2), histology codes (8140-47, 8210-11, 8255-8575), and surgery on primary site code (30). Patients were excluded if they had clinically metastatic disease at diagnosis or if they had in situ disease. Patients undergoing open distal pancreatectomies were also excluded from the analysis.

Variables

Patient-level variables included age, race/ethnicity, sex, Charlson-Deyo Score for comorbid conditions, insurance type, tumor extent, tumor size, nodal status, and receipt of neoadjuvant or adjuvant therapies. Staging was based on the American Joint Committee on Cancer (AJCC) staging manual, 7^{th} edition. Hospital-level variables included facility type (academic: academic research program, or non-academic: community cancer program, comprehensive community cancer program, integrated cancer network program, and others) and annual hospital volumes (average number of open or minimally invasive pancreatic cancer resections performed at a given hospital, averaged over 2004-2013). The cut-off point for a high-volume hospital was defined as 25 according to a previous report. [13] Short-term oncologic outcome was defined as (a) number of lymph nodes harvested and (b) the rate of margin-positive resections. Long-term oncologic outcome was defined as the overall survival.

Statistical methods

All analyses were performed on an intention-to-treat basis. Descriptive statistical analysis was performed and tabulated as medians and interquartile ranges (IQR) for continuous variables, and frequencies with percentages for categorical variables. We compared patient demographics, cancer-specific, and hospital-level characteristics using the Pearson $\chi 2$ test for categorical data and the Kruskal-Wallis test for continuous data. The Fisher test was performed for categorical data when cell counts were less than 30. The proportional hazards assumption was confirmed by review of Schoenfeld residuals as well as graphically. Hazard ratios with their 95% confidence intervals (CI) were reported. Overall survival was calculated from the date of diagnosis until the date of death and reported in months. Kaplan-Meier curves were used to depict survival differences between the two groups. The log-rank test was used to test these differences for statistical significance. Survival data were not available for patients diagnosed in 2013. Survivors were censored at the date of last contact, whereas those who died were censored at the date of death. All analyses were performed using STATA MP Version 14 (StataCorp, College Station, TX).

Results

A total of 704 patients, in 268 hospitals, underwent minimally invasive distal pancreatectomy. Of these, 605 (86%) patients, in 251 hospitals, underwent LDP and 99 (14%) patients, in 54 hospitals, underwent RDP.

Baseline characteristics for LDP and RDP are shown in Table 1. All baseline characteristics were equally distributed across both groups. For hospitals that utilized either technique at least once during the study period, the median number of LDP cases was 1 (range: 1-30; 53%, 1 case; 20%, 2 cases; 27%, >2 cases) and that for RDP cases was 1 (range: 1-15; 57%, 1 case; 32%, 2 cases; 11%, >2 cases). Distribution of LDP and RDP cases by annual hospital volume of all pancreatic cancer resections is demonstrated in Figure 1.

Clinicopathologic and treatment characteristics of patients in the two groups are shown in Table 2. There were no statistical differences in the clinicopathologic characteristics between LDP and RDP.

Table 1. Patient demographics

Characteristics		Laparoscopic (n = 605)	Robotic (n = 99)	*p*-value
Age, years, n (%)	<60	138 (23)	23 (23)	0.93
	60+	467 (77)	76 (77)	
Sex, n (%)	Male	322 (53)	45 (45)	0.15
	Female	283 (47)	54 (54)	
Charlson-Deyo score, n (%)	0	342 (56)	56 (57)	0.69
	1	185 (31)	33 (33)	
	2+	78 (13)	10 (10)	
Race, n (%)	Non-Hispanic white	486 (81)	80 (82)	0.45
	Black	70 (12)	10 (10)	
	Hispanic white	28 (5)	3 (3)	
	NA/PI/Asian/Other	15 (3)	5 (5)	
Insurance, n (%)	Private insurance	197 (33)	32 (32)	0.34
	Government	387 (65)	64 (65)	
	Not insured/other	13 (2)	0 (0)	
Hospital volume, n (%)	< 25 cases	441 (73)	71 (72)	0.81
	> 25 cases	164 (27)	28 (28)	
Facility type, n (%)	Non-academic	201 (34)	29 (31)	0.51
	Academic	391 (66)	66 (69)	

Abbreviations: NA: native Hawaiïans; PI: pacific islanders.

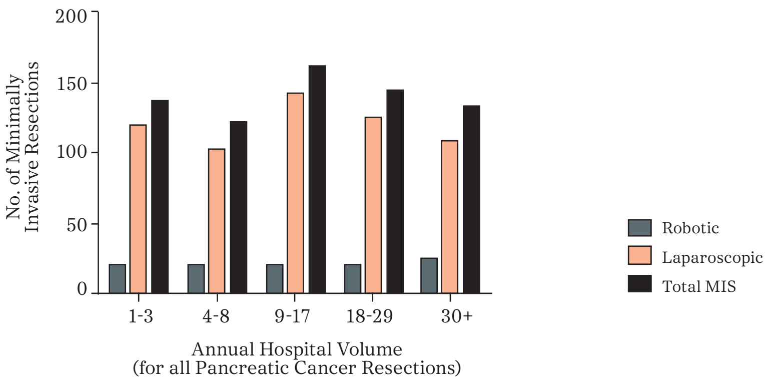

Figure 1. Distribution of minimally invasive distal pancreatic resections across various hospitals grouped by quintiles of annual hospital volume status for all pancreatic resection (minimally invasive or open)

Table 2. Clinicopathologic and treatment characteristics

Characteristics		Laparoscopic (n = 605)	Robotic (n = 99)	*p*-value
Clinicopathologic				
Tumor size, median (IQR), mm		37 (26-50)	35 (24-45)	0.11
Site, n (%)	Body	182 (30)	29 (29)	0.87
	Tail	423 (70)	70 (71)	
AJCC pT-stage, n (%)	T1	66 (11)	12 (12)	0.40
	T2	106 (18)	22 (22)	
	T3	406 (67)	64 (65)	
	T4	12 (2)	0 (0)	
	Tx	14 (2)	1 (1)	
AJCC pN-stage, n (%)	N0	279 (46)	45 (45)	0.10
	N1	301 (50)	45 (45)	
	Nx	25 (4)	9 (9)	
Nodes - positive (if pN1), median (IQR)		2 (1-4)	2 (1-3)	0.19
Grade, n (%)	Low	62 (10)	15 (15)	0.39
	Intermediate	300 (50)	49 (50)	
	High	189 (31)	25 (25)	
	Unknown	54 (9)	10 (10)	
Treatment				
Neoadjuvant therapy, n (%)	None	579 (96)	90 (91)	0.07
	Chemotherapy	16 (3)	7 (7)	
	Chemoradiation	10 (2)	2 (2)	
Adjuvant therapy, n (%)	None	249 (41)	40 (40)	0.82
	Radiation	11 (2)	1 (1)	
	Chemotherapy	221 (37)	40 (40)	
	Chemoradiation	124 (21)	18 (18)	

Abbreviations: AJCC: American joint committee on cancer.

The median follow up was 25 months. There were no differences in the two groups with respect to the oncologic outcomes, as summarized in Table 3. Conversion rate was significantly higher for the laparoscopic approach. Kaplan-Meier survival estimates of patients in the LDP and RDP group were not statistically different. (Figure 2)

Since early years may represent surgeons in the learning curve of robotic surgery, we analyzed differences in the outcomes of robotic cohort over time. We found that the number of robotic and laparoscopic distal pancreatic resections per year increased overtime. (Supplementary Figure 1) On univariate analysis, we found a statistically significant decrease in length of stay with robotic resections overtime. (Supplementary Table 1) There was no difference in number of nodes examined, rate of positive margin resection, conversion to open approach, readmissions or mortality. However, the 1-year overall survival increased overtime.

Discussion

Despite cost constraints and the lack of evidence for oncologic benefit, the national experience with the adoption of the robotic platform for pancreatic cancer resections is increasing. The present study evaluated the comparative effectiveness of RDP vs. LDP for short-term and long-term oncologic outcomes. In addition, we also analyzed postoperative outcomes in this study.

Regarding oncologic outcomes, there are several findings that merit discussion. This is the first study that specifically compares long-term overall survival after minimally invasive distal pancreatectomy between the two modalities. The median follow-up of the cohort was sufficient to reach the median survival after pancreatic adenocarcinoma resection (~25 months). The study failed to demonstrate a difference in overall survival between the two groups. Given the lack of data on overall survival after RDP for pancreatic cancer in the literature, these findings are important. Similarly, there were no differences in the short-term oncologic outcomes such as lymph nodes examined, margin positive rate, and time to adjuvant chemotherapy between the two groups. These findings contradict one study that demonstrated superiority of RDP over LDP with respect to lymph node retrieval and the ability to achieve margin-negative resections, which could be attributed to a type 1 statistical error. [2]

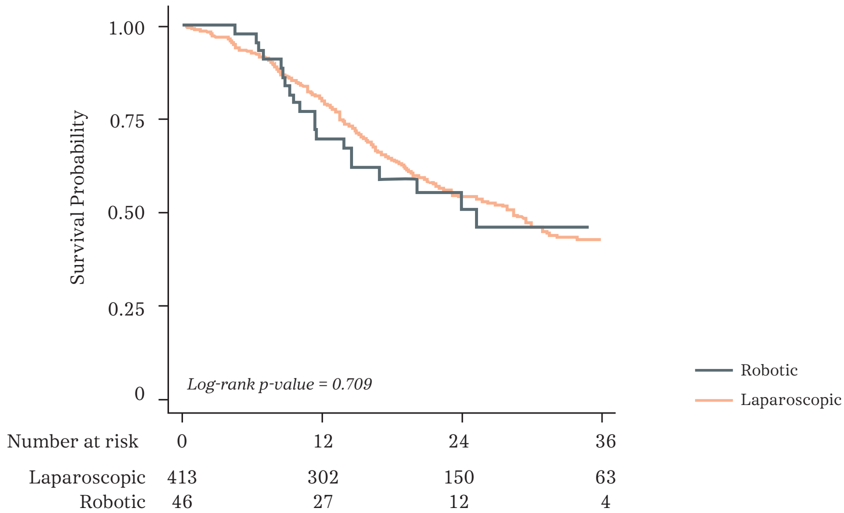

Figure 2. Kaplan-Meier overall survival estimates of patients undergoing minimally invasive distal pancreatectomy (2010-2013) by approach (LDP vs RDP)

Table 3. Outcomes

Characteristics	Laparoscopic (n = 605)	Robotic (n = 99)	*p*-value
Nodes examined, median (IQR)	12 (6-18)	11 (5-20)	0.67
Positive margins, n (%)	93 (15)	16 (16)	0.84
Conversion to open, n (%)	165 (27)	10 (10)	<0.001
Length of stay, median (IQR), days	6 (5-8)	5 (4-7)	0.14
Readmission 30-day, n (%)	57 (9)	9 (9)	0.92
Mortality 30-day, n (%)	7 (1)	0 (0)	0.28
Mortality 90-day, n (%)	16 (3)	0 (0)	0.10
Time to chemotherapy, median (IQR), days	50 (38-65)	52.5 (37-71)	0.65
Overall survival			0.71
1-year	80 (76-84)	70 (53-81)	
2-year	54 (49-59)	51 (34-66)	
3-year	43 (37-48)	46 (28-62)	

Abbreviations: IQR: interquartile range.

12

Regarding postoperative outcomes, the findings of this study are similar to those previously noted in the literature. [10, 11] There were no differences in length of stay, 30-day readmission, or 30-day and 90-day mortality between the two modalities. Of note the NCDB does not record data on operative time or cost, both of which are known limitations of the robotic approach. Additionally, data concerning postoperative complications including pancreatic leak and fistula were not available. These findings are consistent with prior literature that shows no differences in above mentioned metrics. [10, 11] While postoperative mortality, readmissions and length of stay provide crude estimates of safety, without more granular data on complications, generalized safety cannot be comprehensively established based on this study.

The study finds that conversion rates are significantly lower with RDP compared to LDP. This has been observed in prior institutional reports comparing the two approaches. [2, 14] As noted above, this did not translate into a difference in length of stay. Since the reason for conversion is not recorded in the NCDB, it is not possible to explain the difference observed in this analysis. Others have speculated that the reduced conversion with RDP could be attributed to ease of control of hemorrhage with the robotic platform or the ability to progress through the operation that requires challenging dissection as has been established for rectal cancer surgery. [1, 2, 9] Alternatively, the patients are probably highly selected by surgeons who are "pioneering" robotic surgery at their institution and have a vested interest in the operation being completed robotically. It is also possible that the surgeons in the RDP group are highly skilled laparoscopic surgeons who are beyond their learning curve for LDP compared to those in the LDP group (assuming that expertise in laparoscopic skillset improved operative performance on the robotic platform). [15] While we do not have comparative data on individual surgeon experience or the institutional experience with the minimally invasive approach, we note that the two groups were similar with respect to the overall volume of pancreatic cancer resections. Given these limitations, the reduced conversion rate observed in this study should be interpreted with caution.

The trend toward implementing new technology for a complex operation like distal pancreatectomy in low volume centers could be considered worrisome. [16] The majority of hospitals included in this study only performed one RDP (57%) and one LDP (53%) for pancreatic cancer during the study period encompassing four years. Furthermore, approximately 75% of the hospitals performing each of these operations could be considered low volume for any pancreatic resection for cancer. These results are comparable to national trends. For instance, during the same time (2010-2013) 1,342 open distal pancreatectomies were performed within the NCDB cohort. Minimally invasive distal pancreatectomies represented 34.4% (704/2046) of the total distal pancreatectomies for pancreatic cancer. [8] In comparison, Rosales Velderrain et al. compared national trends from two different databases NSQIP and NIS during 2005-2010. They identified that minimally invasive approach was used in 15-27% of patients. Further, 59-66% of the time it was performed for malignancy. [17] In another analysis of NIS (1998-2009) by Tran Cao et al. even lower proportion of cases (7.3% in year 2009) were performed with a minimally invasive approach. [18] Our study period does not extend beyond 2013 but suggests a rising trend in the adaptation of minimally invasive approach. It is likely that much higher proportion of distal pancreatectomies today, are being performed in a minimally invasive fashion. A comparison of outcomes of minimally invasive approach by hospital volume is beyond the scope of this study. However, the low mortality with either approach suggests that patients in both groups were highly selected.

The findings of the study should be interpreted with caution given its retrospective design. While the baseline characteristics were comparable between the two groups, not all factors are accounted for. For instance, there was no information on surgeon experience in the database which could impact outcomes. However, the groups were compared on many factors that determine oncologic and postoperative outcomes. Secondly, while the oncologic outcomes are similar between the two groups, the study was not powered to conclude non-inferiority of survival which would require a much larger sample size. Thirdly, the study did not include a comparison of cost-effectiveness of the two approaches. A recent study from France demonstrated that these costs were marginally higher for the robotic approach (€13,611 vs. €12,509, $p < 0.001$) compared to the laparoscopic approach. [19] In comparison, a study from Spain demonstrated no significant difference (RDP: €9,198.64 vs LDP: €9,399.74; $p > 0.5$) between the two approaches. [20] Waters et al. reported that the cost of RDP was lower ($10,588) compared with the laparoscopic ($12,986) procedure because of a shorter length of stay. [21] Kang et al. found RDP to be 2.5 times more expensive than LDP ($8,304 vs. $3,861). [22] Finally, Butturini et al. also found RDP to be more expensive compared with LDP (€ 2.700-3.190 vs. €1,434-1,674). [1] Taken collectively, cost is a significant constraint for adaptation of robotic surgery at present. Cost of instrumentation, longer operative times, personnel and suboptimal workflows all contribute to these costs and are not completely captured in the above-mentioned studies. [23] However, in the near future, several other companies are expected to bring their surgical robotic system on the market. Hence, the costs are expected to decrease significantly. The decision to perform RDP over LDP, therefore, will ultimately depend on the comparative effectiveness of the two modalities and the surgeon's skillset.

Conclusion

In conclusion, this nationwide retrospective study found similar short-term and long-term oncologic outcomes between highly selected, well-balanced RDP and LDP cohorts. Similarly, postoperative outcomes were comparable for the two approaches with potentially a lower conversion rate for the robotic approach. Considering the limitations of a retrospective design, future prospective studies should further investigate the clinical benefit of the use of a robotic system compared to conventional laparoscopy in distal pancreatic resections.

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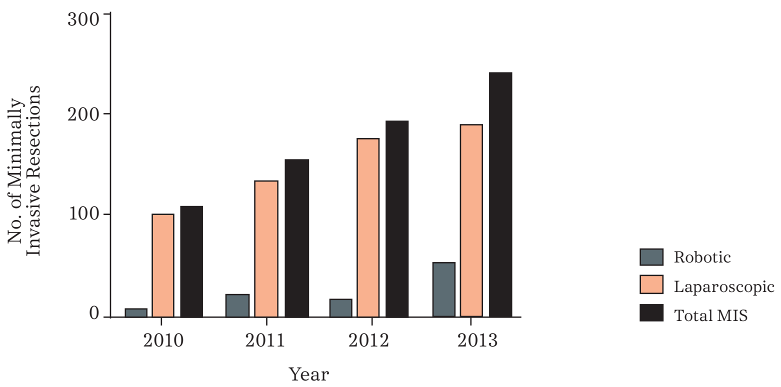
Appendix - Supplementary material Chapter 12

Supplementary Table 1. Outcomes of robotic distal pancreatectomy 2010-2013

Characteristic	2010, (n=6)	2011, (n=22)	2012, (n=18)	2013, (n=53)	*p*-value
Nodes examined, median (IQR)	7 (7-19)	8 (2-16)	13 (6-29)	14 (6-19)	0.23*
Positive margins, n (%)	1 (17)	4 (18)	2 (11)	9 (17)	0.93~
Conversion to open, n (%)	1 (17)	3 (14)	0 (0)	6 (11)	0.44~
Length of stay, median (IQR), days	6 (4-7)	5 (4-8)	5 (4-7)	5 (4-7)	<0.001*
Readmission 30-day, n (%)	0 (0)	3 (14)	1 (6)	5 (9)	0.69~
Mortality 30-day, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	N/A
Mortality 90-day, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	N/A
Time to chemotherapy, median (IQR), days	52 (52-52)	41 (27-53)	56 (35-74)	51 (40-71)	0.31*
Overall survival, 1-year (95% CI)	17 (0.7-52)	67 (42-82)	94 (65-99)	N/A	<0.001#

Abbreviations: IQR: interquartile range; N/A: not applicable. Legend: *One-way ANOVA; ~ Fisher-exact test, # log-rank test.



Supplementary Figure 1. Trends in the adaptation of minimally invasive (MIS) distal pancreatectomy for pancreatic cancer from 2010-2013

Part 3

Summary and General Discussion

Chapter 13

Summary

13

Summary

Hepato-pancreato-biliary (HPB) surgery includes all surgical procedures to the liver, bile ducts and pancreas and can be highly complex, associated with high morbidity and mortality. To mitigate the impact of the surgery on the patient, conventional laparoscopy was introduced. This technique, however, is limited by the non-articulating instruments and two-dimensional view. These restrictions do not make laparoscopy suited for the entire spectrum of HPB surgery. The use of a surgical robot provides a potential solution with three-dimensional view, a magnified view of the operative field, scaled movements and articulating instruments. Potentially, the use of the surgical robot broadens indications for minimally invasive HPB surgery. Research presented in this thesis evaluated the different aspects of the set-up, technical details, dissemination and outcomes of robotic liver surgery (part 1) and robotic pancreatic surgery (part 2).

Part 1 - Robotic liver resection

Chapter 2. Systematic review and meta-analysis on robotic liver resection

In chapter 2 we have provided a literature overview of the indications, procedural details and short-term surgical outcomes of robotic liver resection. Pooled results from twelve, mostly retrospective studies showed that the procedure is feasible and safe in selected patients, with acceptable surgical outcomes. In addition, we performed a pooled analysis of three separate groups of resections, based on the Louisville Statement on laparoscopic liver surgery: minor resections of the anterolateral segments (2, 3, 4B, 5, 6), minor resections of the posterosuperior segments (1, 4A, 7, 8) and major resections (≥ 4 segments). Results from this second analysis demonstrated that robotic liver resection is safe and feasible for all of these categories, with low conversion rates and no mortality. However, patients in the included studies were selected en total numbers remained small.

Chapter 3. The set-up of a robotic liver surgery program

The set-up of a robotic liver surgery program requires several prerequisites, as described in chapter 3, against the background of the UMC Utrecht experience. First, a dedicated team consisting of surgeons, anesthesiologists, OR staff and robotic support staff is a key element in the set-up of a successful program. Second, equipment and available expertise are needed. There has been a robotic surgical system since 2000 in the UMC Utrecht, mainly used for urologic and gastrointestinal procedures (esophagectomies, thyroidectomies and distal pancreatectomies). Third, proctoring is essential in such complex procedures. Further, in this chapter all aspects of starting up robotic liver surgery are discussed, ranging from patient selection, anesthesia and preoperative care, learning curves to cost and healthcare context.

Chapter 4. Initial experience robotic liver surgery

In chapter 4 the surgical outcomes of the first sixteen robotic liver resections performed in the UMC Utrecht between August 2014 and March 2016 are presented, including eight patients who underwent a resection of a posterosuperior segment. Complication rates in this initial series were acceptable: solely four patients suffered from a major complication (defined as ≥ Clavien-Dindo grade III) and there was no mortality. One procedure (resection of segment 5) was converted to a laparotomy since a safe oncologic could not be assured in the fibrotic/cirrhotic hepatic parenchyma. Results of this initial series demonstrate feasibility of the technique, also for resections of the posterosuperior segments.

Chapter 5. Robotic versus open liver resections of the posterosuperior segments

In chapter 5 we further focused on minor resections of the posterosuperior segments; the group of resections for which we hypothesized that the use of robotic technology is beneficial in particular. Conventional laparoscopy appears not to be well suited for resections of these ill-located segments and most of these resections were still performed through open surgery by the time of this study. Hence, in this study we compared minor (≤ 3 segments) robotic resections to minor open resections of the posterosuperior segments. Data from four expert centers worldwide (Memorial Sloan Kettering Cancer Center, City of Hope Comprehensive Cancer Center, Yonsei University Health System and the University Medical Center Utrecht) were collected. Robotic resections of these segments were compared to their open counterpart, before and after propensity score matching. Results from the analyses after propensity score matching demonstrated comparable perioperative outcomes but a decrease in length of stay by half in favor of the robotic approach; indicating a much faster recovery after the minimally invasive approach.

Chapter 6. Techniques for parenchymal transection techniques in robotic liver resection

Several techniques for parenchymal transection during robotic liver resection are discussed in chapter 6. Which technique should be used for transection of the hepatic parenchyma remains under debate in open and laparoscopic liver surgery. Hence, naturally, in robotic liver resection there is no consensus yet on which technique is best suited for transection of the hepatic parenchyma. In this chapter the surgical details and short-term outcomes of 70 robotic liver resection are presented, during which the Vessel Sealer (Extend) (Intuitive Surgical Inc., Sunnyvale, CA, USA) was used primarily for parenchymal transection. Results from this study demonstrate that the use of the Vessel Sealer device for parenchymal transection during robotic liver surgery is feasible and provides adequate surgical outcomes. There were no patients who suffered from postoperative bleeding and just three patients (4%) had postoperative bile leakage. However, one should keep in mind that the majority of the resections in this study were minor resections (n= 60, 86%).

Chapter 7. Video chapter - robotic right hepatectomy and robotic resection of segment 7

This chapter contains two video articles of robotic liver resections. The first video demonstrates robotic right hepatectomy with dissection of the variant right hepatic pedicles for a centrally located liver tumor. The patient was a 77-year-old male with a liver tumor in segment 5/8 with concurrent biliary dilation that was detected on a CT-scan made in the course of his cardiac history. This video eminently demonstrates the benefits of the increased surgical dexterity of the robotic system, which come in handy when operating in the hilum of the liver.

The second video contains a stepwise description of robotic liver resection of segment 7, covering patient positioning, trocar placement and a detailed description the surgical steps. Again, this video illustrates the feasibility of robotic resection of segment 7 and the benefits of the improved vision and wristed instruments in resections of ill-located lesions.

Part 2 - Robotic pancreatic resection

Chapter 8. Developing a robotic pancreas program

In chapter 8, following the example of chapter 3, the set-up and prerequisites for a robotic pancreas program are described, against the background of the nationwide Dutch experience, mainly focused on pancreatoduodenectomy. All different aspects of the set-up of a program are discussed including patient selection, anesthesia and preoperative care and tips and tricks. The main focus of this chapter, however, is training. Surgeons in the UMC Utrecht performed the first robotic pancreatoduodenectomy in the Netherlands in 2016, after following training according to the University of Pittsburgh Medical Center (UPMC) protocol. This initial experience in Utrecht led to the initiation of LAELAPS-3, a nationwide Dutch Pancreatic Cancer Group (DPCG) training program for robotic pancreatoduodenectomy. Training in this program is based on simulation training, suturing and anastomoses training on artificial organs, video training and proctoring of the first procedures. The different components of LAELAPS-3 are extensively described in this chapter.

Chapter 9. Dissemination of robotic HPB surgery in a larger group of surgeons

Chapter 9 describes the dissemination of robotic HPB surgery in a group of surgeons and summarizes outcomes of robotic liver resections and robotic pancreatoduodenectomies. Five surgeons were consecutively introduced to robotic HPB surgery. Mean operative time for the robotic liver resections was 160±78 minutes. Mean operative time for the robotic pancreatoduodenectomies was 420±67 minutes. Operative times remained stable over time and were not affected by the introduction of new surgeons. Stepwise implementation and expansion of robotic HPB surgery within one center is feasible and associated with good clinical outcomes. Despite introducing new surgeons to the technique, operative times, an indicator of the learning process, remained stable over time.

Chapter 10. Video chapter - Robotic pancreatoduodenectomy in a 10-year-old child

A robotic approach to pancreatoduodenectomy might be especially in patient with premalignant or benign lesions, since these patients have a long life expectancy and might benefit in particular from the long-term advantages of a minimally invasive approach such as fewer major abdominal hernias, fewer adhesive small bowel obstructions, and improved cosmesis. This video is an example of such a case. The patient was a ten-year-old child with a solid pseudopapillary neoplasm in the pancreatic head for which a pancreatoduodenectomy was indicated. This video highlights several aspects of robotic pancreatoduodenectomy in a child, including port placement, patient positioning and the surgical steps of robotic pancreatoduodenectomy.

Chapter 11. The first 100 robotic pancreatoduodenectomies in the Netherlands

In this chapter the results of the first 100 robotic pancreatoduodenectomies in the Netherlands are presented. Data from three centers (Erasmus Medical Center Rotterdam, Maasstad Hospital Rotterdam and Regional Academic Cancer Center Utrecht, locations: UMC Utrecht and St. Antonius Hospital) were collected from prospectively maintained databases and analyzed *post hoc*. Results from this first 100 procedures were promising: there were solely 22 patients (22%) with a severe complication, nineteen patients (19%) with a postoperative pancreatic fistula (ISGPS gr. B/C), nine patients (9%) with a postpancreatectomy hemorrhage (ISGPS gr. B/C), two patients (2%) with new-onset multiple organ failure and none of the patients died postoperatively. To put the results of these first 100 procedures in perspective, we additionally performed a systematic review on large (> 500 procedures), recent (published last five years), cohort studies on open pancreatoduodenectomy. We included fourteen studies together containing the results of 12,708 open pancreatoduodenectomies. In these fourteen studies pooled mortality was 3%, pooled morbidity was 38%, pancreatic fistula occurred in 15% of the patients and 7% of the patients suffered from postpancreatectomy hemorrhage. The results from this meta-analysis showed that the results of the first 100 robotic pancreatoduodenectomies in the Netherlands were comparable to the outcomes of open pancreatoduodenectomies.

Chapter 12. Robotic versus laparoscopic distal pancreatectomy - a National Cancer Database analysis

Conventional laparoscopy appears to provide a safe and feasible approach to perform minimally invasive distal pancreatectomy. Though, robotic surgery has been employed in minimally invasive distal pancreatectomy as well. The precise dissection facilitated by the articulating robotic instrumentation and enhanced visualization may confer oncologic benefits, such as an increased number of lymph nodes yielded and an increased percentage of R0 resections. In this chapter we have compared short-term and long-term oncologic outcomes of robotic and laparoscopic distal pancreatectomy for patients who underwent distal pancreatectomy for pancreatic adenocarcinoma in the United Stated between 2010-2013 using the National Cancer Database. In total, there were 704 eligible patients, from which 605 (86%) underwent conventional laparoscopic distal pancreatectomy and 99 (14%) underwent robotic distal pancreatectomy (14%). When comparing laparoscopic distal pancreatectomy with robotic distal pancreatectomy, there was no difference in the percentage of positive margins (15% vs. 16%, $p = 0.84$), the number of lymph nodes examined (12 vs. 11, $p = 0.67$) and overall survival (HR: 1.1, 95% CI: 0.7-1.7; 28 vs. 25 months, $p = 0.71$). However, the percentage of converted procedures was significantly higher in the laparoscopic group (27% vs. 10%, $p < 0.001$).

Chapter 14

General Discussion and Future Perspectives

Discussion and Future Perspectives

Minimally invasive surgery has been developed to alleviate the impact of surgery on the patient and enhance recovery. After the initial reports on the use of conventional laparoscopy decades ago, laparoscopy has been subject to further maturation and technical innovation. Notwithstanding, robotic surgery was introduced as an alternative to conventional laparoscopy and gradually found its way into complex gastrointestinal procedures, such as HPB surgery. At present, the exact role of robotic surgery in liver and pancreatic surgery has not been fully established. Research presented in this thesis provides insight in the initiation, dissemination, technical aspects and initial outcomes of robotic liver surgery (part 1) and robotic pancreatic surgery (part 2). Implications for the current clinical practice, relevance of the research findings and future perspectives are further discussed here.

Robotic liver resection

Recently, the first randomized controlled trial comparing laparoscopic parenchymal-sparing liver resection with open liver resection for colorectal liver metastases was published by Fretland et al. [1] This trial demonstrated patient benefits of the laparoscopic approach, such as a decrease in complication rate by 12% (19% laparoscopic versus 31% open, $p = 0.021$) and shorter length of hospital stay. Similar advantages of the laparoscopic approach were shown in other non-randomized studies. [2, 3] Nonetheless, widespread implementation of the technique has lagged behind for HPB surgery. The advent of robotic surgery in minimally invasive liver resection appears to have been giving impetus to the field of minimally invasive liver surgery. In the Netherlands, for example, the percentage of liver resections performed through minimally invasive surgery has increased from 6% in 2011 to 23% in 2016. [4]

Results from **Chapter 2**, a systematic review and meta-analysis of the literature on robotic liver resection, demonstrated the relative novelty of the technique by the time of the start of this thesis, with ‘only’ 12 studies describing 363 patients undergoing robotic liver resection available in the literature. Results from studies in the first part of this thesis demonstrate the feasibility and safety of robotic liver resection, for all three categories of resections: minor resections of the anterolateral segments, minor resections of the posterosuperior segments and major resections (> 3 hepatic segments), as defined in the

Louisville Statement. [5] Throughout the first part of this thesis we hypothesized that the use of robotic technology might especially be beneficial in the group of minor liver resections of the posterosuperior segments, as highlighted in **Chapter 5** of this thesis. In this chapter, the robotic approach reduced the length of stay by half compared to open approach liver resection, indicating a much faster recovery. One should keep in mind, however, that this study was limited by its retrospective nature and the inherent risk of bias, although we aimed to minimize this risk by using propensity score matching.

We addressed the set-up, dissemination, technical aspects and initial outcomes of robotic liver surgery in the first part of this thesis. Since robotic liver surgery is in its infancy, there are still aspects to the technique that remain open for discussion.

One of the most important questions that remain is: what evidence is needed to definitively justify the use of robotic technology in liver resection? To date, no randomized controlled trials have been conducted comparing robotic liver resection to its laparoscopic or open counterpart. A randomized controlled study design is considered the gold standard to justify the use of a surgical technique. One could contemplate if robotic liver surgery should be proven superior in a randomized controlled trial to justify its further implementation or, since the technique seems to be a natural evolution of conventional laparoscopy and intuitively less impactful than open surgery, that no randomized data are needed? Therewith, the question is sparked what the timing of such a trial should be, if indicated at all? There is an inherent learning curve to robotic liver resection, which could bias the results if a trial is conducted in a too early stage, which, for example, possibly preceded the unfavorable outcome of the LEOPARD-II trial. [6] On the other hand, when the surgical technique has been employed for a while, there might not be equipoise anymore. Buxton's Law, which states: '*it's always too early (for rigorous evaluation) until it's suddenly too late*' seems to pose a challenge for surgical trials. [7] Further, one could argue that the outcome of such a randomized controlled trial should permanently discard one of the compared techniques. This depends, however, partially on the primary focus. For example, a slight difference in time to functional recovery of postoperative length of stay would probably not withhold surgeons from using a surgical technique. By contrast, a difference in major morbidity or mortality probably would. It remains open for debate if a randomized controlled trial is the designated study design to demonstrate this.

In addition, a systematic review and recent survey amongst The European Surgical Association (ESA) members demonstrated that surgical randomized controlled trials (RCTs) appeared to have a moderate impact on daily surgical practice. In this study, it was recommended that other tools to evaluate surgical innovations besides RCTs should be explored as well. [8]

Robotic surgery remains under scrutiny, mostly because critics do not find the current evidence sufficient enough to compensate the higher costs of robotic surgery. Purchase and maintenance are indeed more expensive than for conventional laparoscopy. [9] However, the discussion on costs seems not to be entirely finished. For example, in the Netherlands there is currently no specific diagnosis treatment combination for robotic procedures (‘DBC healthcare product’), hence hospitals are left responsible for the additional costs of the robotic technology. This is expected to change in the coming years. Also, more companies are expected to bring their surgical robotic to the market in the next few years, which will stimulate competitive pricing and decrease costs.[10]

Taken together, the advent of robotic liver resection has expanded indications for minimally invasive liver resection. The increased surgical dexterity comes out especially well in resections of the posterosuperior segments or during meticulous hilar dissection, but robotic liver surgery is also safe and feasible for minor resections of the anterolateral segments or major resections, as demonstrated in **Chapter 7**. Robotic technology will probably not fully replace laparoscopic liver resection, at least not in the next few years, since laparoscopy might be perfectly suited for minor resections of the anterolateral segments.

Safety and feasibility of robotic liver resection has been demonstrated in this thesis. Probably, no randomized data are needed for further expansion of the technique. Future research should rather focus on prospective registries to monitor surgical outcomes, patient selection, optimizing surgical techniques and training surgeons and residents.

Robotic pancreatic surgery

Pancreatic surgery was one of the last procedures that was embarked on minimally invasively. Traditionally, pancreatic surgery is complex with a high risk of complications. Although, surgical morbidity and mortality after pancreatic resection were reduced significantly the past decades, major morbidity and mortality in the Netherlands still linger approximately around 30% and 4%, respectively. [11] As for liver resection, minimally invasive surgery was introduced to mitigate the impact of surgery on the patient.

Robotic pancreatoduodenectomy

After initial safe implementation in the Netherlands with adequate results of 114 laparoscopic pancreatoduodenectomies, laparoscopic pancreatoduodenectomy was compared to its open counterpart in a randomized controlled trial. [6, 12] This study was discontinued prematurely due to safety concerns regarding the laparoscopic approach, after which laparoscopic pancreatoduodenectomy was no longer allowed in the Netherlands. Several potential explanations were given for this unfavorable and unexpected outcome, including a lack of volume in some participating centers and the fact that the technique has a long learning curve. In part 2 of this thesis we hypothesized that the increased surgical dexterity of the robotic system would make the use of the surgical robot optimally suited for a technically complex procedure such as pancreatoduodenectomy.

The University of Pittsburgh Medical Center (UPMC), was the first hospital in the United Stated to develop and standardize robotic pancreatoduodenectomy. To date, several hundred procedures have been performed in UPMC and procedural outcomes are promising. [13] Following the example of the UPMC, robotic pancreatoduodenectomy was initiated in UMC Utrecht in 2016. The first procedures were proctored by a surgeon from this American expert center and their surgical protocol was used, as described in **Chapter 8**. After Utrecht, several other centers in the Netherlands also initiated a robotic pancreatoduodenectomy program. Results from the first 100 robotic pancreatoduodenectomies in the Netherlands from three centers are presented in **Chapter 11**. This study demonstrated safety and feasibility of the technique. Additionally, a meta-analysis showed that our results were at least non-inferior compared to results of several recent, large series on open pancreatoduodenectomy. The percentage of patients with a grade B/C pancreatic fistula seemed relatively high in this study. However, this can be explained (at least partially) by the recent changes in complication management strategies, since patients undergo minimally invasive drainage of intraabdominal fluid collections with a lower threshold to prevent more severe illness and potential organ failure. On the contrary, robotic pancreatoduodenectomy is still a relatively new procedure and surgical techniques for the construction of the pancreaticojejunostomy might change and improve pancreatic fistula rates.

The robotic system allows the surgeon to operate with the same dexterity as in open surgery, which cannot be achieved using conventional laparoscopy. The optimized surgical dexterity during robotic pancreatoduodenectomy is illustrated in **Chapter 10**: a video of a robotic pancreatoduodenectomy in a ten-year-old child with a solid pseudopapillary neoplasm. Using robotic technology for pancreatoduodenectomy might be especially beneficial for the growing group of patients with premalignant or benign lesions that have to undergo pancreatoduodenectomy. These patients have a long life expectancy and might benefit the most from the long term benefits of a minimally invasive approach such as fewer major abdominal hernias, adhesive small bowel obstructions and improved cosmesis.

As for liver resection, for robotic pancreatoduodenectomy the question remains what level of evidence is needed to justify the use of robotic technology in pancreatic resection. The same aforementioned pros and cons on whether to perform a randomized controlled trial in robotic liver surgery are more or less applicable to pancreatoduodenectomy. We have demonstrated safety of the procedure, the added value of a randomized controlled trial remains debatable. Also, when setting up a randomized study, which technique should be employed as the control arm? And at which point in time should we perform such a trial?

Outcomes should be monitored prospectively to ensure safe expansion of the technique. Since more and more surgeons are willing to start robotic pancreatoduodenectomy future research should also focus on training and safely implementing robotic pancreatoduodenectomy in other hospitals, although one could debate whether such a complex surgery shouldn't be more centralized and should be reserved for high volume expert centers.

Robotic distal pancreatectomy

In contrast to pancreatoduodenectomy, the added benefit of robotic technology might not be as clear in distal pancreatectomy as in pancreatoduodenectomy. Construction of the anastomoses after pancreatoduodenectomy (pancreaticojejunostomy, hepaticojejunostomy and gastrojejunostomy) is facilitated greatly by the increased visibility and wristed instruments. This might be less the case in distal pancreatectomy. Safety and feasibility of a laparoscopic approach to distal pancreatectomy have been convincingly demonstrated in the LEOPARD-I trial, and other studies. [14] The use of robotic technology in this procedure might depend on a surgeon's preference and experience with robotic or laparoscopic surgery. The increased robotic dexterity does have some benefits in distal pancreatectomy including fewer conversions, as demonstrated in **Chapter 12**, a National Cancer Database study.

Conclusion

The use of robotic technology in HPB surgery seems feasible and safe and provides a higher level of surgical dexterity than conventional laparoscopy. These benefits are most outspoken in procedures that require extensive suturing, such as pancreatoduodenectomy, or in hilar dissection or resections of the posterosuperior segments in liver resection. Using robotic technology, indications for minimally invasive liver and pancreatic resection are extended, with technical benefits such as fewer conversions to laparotomy needed. Still, conventional laparoscopy will in all likelihood not disappear soon since some technically 'easier' aspects of HPB surgery, such as liver resections of the anterolateral segments or distal pancreatectomy, can be embarked on using conventional laparoscopy, dependent on the surgeon's preference, previous experience with robotic or laparoscopic surgery and the availability of a robotic system. To justify further implementation and expansion of robotic HPB surgery, prospective registries should be maintained to ensure safety of the procedures. Randomized data will likely not be essential for further dissemination and future research should rather focus on training surgeons and residents for robotic HPB surgery and continuous outcome assessment through clinical audits and registries. Although the surgical robot in its current form may further evolve and may continue to change, minimally invasive surgery with wristed instruments and three-dimensional vision is here to stay.

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Appendices

Summary in Dutch
Nederlandstalige Samenvatting

Hepato-pancreato-biliaire (HPB) chirurgie omvat het gehele scala aan operaties aan de lever, galwegen en het pancreas en kan hoogst complex zijn, geassocieerd met een hoge morbiditeit en mortaliteit. Om de impact van dergelijke operaties op de patiënt te verminderen is conventionele laparoscopie geïntroduceerd. Echter, deze techniek wordt beperkt door de niet-articulerende instrumenten en de tweedimensionale visus en is hierdoor niet geschikt voor gehele spectrum van HPB chirurgie. Het gebruik van de operatierobot biedt hier mogelijk uitkomst. De instrumenten van de operatierobot zijn articulerend, de bewegingen geschaald en het beeld van het operatiegebied is driedimensionaal. Mogelijk kunnen meer operaties aan de lever en het pancreas minimaal invasief uitgevoerd worden door het gebruik van de operatierobot. Het onderzoek gepresenteerd in dit proefschrift biedt inzicht in de verschillende aspecten van de opzet, de uitbreiding, chirurgisch-technische details en de uitkomsten van robot-geassisteerde leverchirurgie (deel 1) en robot-geassisteerde pancreaschirurgie (deel 2).

Deel 1 - Robot-geassisteerde leverchirurgie

Hoofdstuk 2. Systematisch literatuuronderzoek naar robot-geassisteerde leverresecties

In hoofdstuk 2 hebben wij een systematisch literatuuronderzoek verricht naar de indicaties, procedurele details en korte-termijn chirurgische uitkomsten van robot-geassisteerde leverresecties. Gepoolde resultaten van twaalf, met name retrospectieve, studies laten zien dat de procedure haalbaar en veilig is voor geselecteerde patiënten, met acceptabele chirurgische uitkomsten. Aanvullend hebben wij een analyse verricht waarbij wij de resecties onderverdeelden in drie groepen, gebaseerd op de groepen beschreven in de Louisville Statement over laparoscopische leverchirurgie: kleine resecties van de anterolaterale segmenten (2, 3, 4B, 5, 6), kleine resecties van de posterosuperieure segmenten (1, 4A, 7, 8) en majeure resecties (≥ 4 segmenten). De resultaten van deze secundaire analyse laten zien dat robot-geassisteerde leverchirurgie veilig en haalbaar is voor al deze drie groepen, met lage conversie percentages en geen mortaliteit. Echter, patiënten in de geïncludeerde studies zijn geselecteerd en de totale aantallen patiënten zijn relatief klein.

Hoofdstuk 3. De opzet van een programma voor robot-geassisteerde leverchirurgie

Beginnen met robot-geassisteerde leverchirurgie verreist enkele aanpassingen en randvoorwaarden in een ziekenhuis, welke zijn beschreven in hoofdstuk 3 aan de hand van de ervaringen in het UMC Utrecht. Ten eerste, een toegewijd team bestaande uit chirurgen, anesthesiologen, OK personeel en ondersteunend technisch personeel is essentieel voor het opstarten van een succesvol programma. Ten tweede zijn het juiste materiaal en reeds aanwezige expertise nodig, zoals in het UMC Utrecht. Hier staat sinds 2000 een operatierobot, welke voor urologische en andere gastro-intestinale procedures (oesofagusresectie, thyreoidectomie en distale pancreatectomie) al gebruikt werd. Ten derde, proctoring van dergelijk complexe procedures is van zeer groot belang. In dit hoofdstuk worden deze eerdergenoemde aspecten uitgebreid belicht en worden ook de patiëntselectie, anesthesiologische aspecten van de procedure, leercurves en de kostenaspecten bediscussieerd.

Hoofdstuk 4. Initiële resultaten van robot-geassisteerde leverresecties

In hoofdstuk 4 worden de initiële resultaten van de eerste zestien robot-geassisteerde leverresecties gepresenteerd die uitgevoerd werden tussen augustus 2014 en maart 2016 in het UMC Utrecht. Hierbij zitten acht patiënten die een resectie van een posterosuperieur segment ondergingen. Het aantal complicaties is acceptabel: slecht vier patiënten hadden een majeure complicatie (gedefinieerd als ≥ Clavien-Dindo graad III) en er was geen mortaliteit. Eén procedure werd geconverteerd naar een laparotomie. Dit betrof een resectie van een hepatocellulair carcinoom in segment 5. Peroperatief kon een veilige oncologische marge niet gewaarborgd worden door het fibrotische/cirrhotische aspect van het leverweefsel. Resultaten van deze initiële serie tonen aan dat de procedure inderdaad veilig en haalbaar is, ook voor resecties van de posterosuperieure segmenten.

Hoofdstuk 5. Robot-geassisteerde versus open leverresecties van de posterosuperieure segmenten

In hoofdstuk 5 hebben wij gefocust op de kleine resecties (≤ 3 segmenten) van de posterosuperieure segmenten. Wij hadden de hypothese dat het gebruik van de operatierobot met name voordelig was voor deze groep resecties. Conventionele laparoscopie lijkt geen geschikte operatietechniek voor resecties van deze segmenten. Hierdoor werden ten tijde van deze studie de meeste van deze resecties nog uitgevoerd middels open chirurgie. Vandaar hebben wij in deze studie kleine, open resecties van de posterosuperieure segmenten vergeleken met kleine, robot-geassisteerde resecties van deze segmenten. Data werden verzameld in vier expertise centra wereldwijd: Het UMC Utrecht (Utrecht, Nederland), City of Hope Comprehensive Cancer Center (Los Angeles, USA), Yonsei University Health System (Seoul, Zuid-Korea) en het Memorial Sloan Kettering Cancer Center (New York, USA). Robotoperaties werden vergeleken met open operaties, voor en na propensity score matching. Resultaten van de analyse na propensity score matching lieten vergelijkbare operatieve details en postoperatieve uitkomsten zien, echter was de opnameduur in de robot groep gehalveerd ten opzichte van de open groep; wijzend op een sneller herstel na de robotoperatie.

Hoofdstuk 6. Technieken voor parenchym transsectie in robot-geassisteerde leverresecties

Technieken voor transsectie van het leverparenchym tijdens robot-geassisteerde leverresecties worden behandeld in hoofdstuk 6. In open leverchirurgie en in laparoscopische leverchirurgie bestaat er nog geen duidelijk superieure techniek voor transsectie van het parenchym. Ook voor robot-geassisteerde leverresecties is niet duidelijk welke techniek of welk apparaat gebruikt zou moeten worden voor de parenchym transsectie. In dit hoofdstuk worden de chirurgische details en postoperatieve uitkomsten van 70 robot-geassisteerde leverresecties gepresenteerd. Tijdens al deze procedures werd de Vessel Sealer (Extend) (Intuitive Surgical Inc., Sunnyvale, CA, USA) gebruikt voor de parenchym transsectie. Resultaten van deze studie laten zien dat het gebruik van de Vessel Sealer veilig en haalbaar is voor transsectie van leverparenchym in robot-geassisteerde leverresecties en geassocieerd met adequate uitkomsten. Er waren geen patiënten met een postoperatieve bloeding en er waren slecht drie patiënten (4%) met gallekkage postoperatief. Echter, het grootste deel van de resecties in deze studie waren kleine leverresecties (n = 60, 86%).

Hoofdstuk 7. Video hoofdstuk - robot-geassisteerde hemihepatectomie rechts en segment 7 resectie

Hoofdstuk 7 bevat twee video's van robot-geassisteerde leverresecties. De eerste video betreft een robot-geassisteerde hemihepatectomie rechts in een 77 jaar oude patiënt. Deze patiënt onderging een CT-scan in het kader van een follow-up traject bij de cardiologie. Hierop werd een afwijking is segment 5/8 gezien en dilatatie van de galwegen. Deze video laat de verschillende stappen van een robot-geassisteerde hemihepatectomie rechts zien voor een centrale levertumor met dissectie van de leverhilus en de rechter lever pedikels. De technische voordelen van de operatierobot zorgen voor optimale chirurgische behendigheid, voordelig bij dissectie van de lever hilus, zoals geïllustreerd in deze video.

De tweede video bevat een stapsgewijze beschrijving van een robot-geassisteerde segment 7 resectie, waarin patiënt positionering, trocar plaatsing en een gedetailleerde beschrijving van de verschillende stappen van de operatie behandeld worden. Deze video toont opnieuw aan dat het gebruik van de operatierobot, met de verbeterde visus en articulerende instrumenten, voordelig is tijdens resecties van deze moeilijk gelegen afwijkingen.

Deel 2 - Robot-geassisteerde pancreaschirurgie

Hoofdstuk 8. Opstarten van een robot pancreas programma

In hoofdstuk 8, in navolging op hoofdstuk 3, wordt de opzet van een robot pancreas programma uiteengezet aan de hand van de landelijke ervaringen in Nederland, gericht op de robot-geassisteerde pancreatoduodenectomie. De verschillende kanten van de opzet van een robot pancreas programma zoals patiënt selectie en de anesthesiologische en perioperatieve zorg worden belicht. Echter, de belangrijkste focus van dit hoofdstuk is training. De eerste robot-geassisteerde pancreatoduodenectomie in Nederland is in 2016 in het UMC Utrecht verricht. De chirurgen uit het UMC Utrecht bereidden zich hierop voor door chirurgische training volgens het University of Pittsburgh Medical Center (UPMC) protocol. In navolging hierop werd het landelijke Dutch Pancreatic Cancer Group (DPCG) 'LAELAPS-3' trainingsprogramma voor robot-geassisteerde pancreatoduodenectomie ontwikkeld. Training binnen LAELAPS-3 bestaat uit simulatie training, hechtoefeningen, het reconstrueren van anastomosen op artificiële organen, video training en proctoring van de eerste procedures. De verschillende onderdelen van LAELAPS-3 worden in hoofdstuk 8 toegelicht.

Hoofdstuk 9. Uitbreiding van robot-geassisteerde lever- en pancreaschirurgie binnen een grotere groep chirurgen

In hoofdstuk 9 wordt de verdere uitbreiding van robot-geassisteerde HPB chirurgie binnen een grotere groep chirurgen beschreven. Ook worden de uitkomsten van de robot-geassisteerde lever- en pancreasresecties die zijn uitgevoerd in dit chirurgische programma samengevat. Vijf HPB chirurgen werden stapsgewijs geïntroduceerd in de robot-geassisteerde HPB chirurgie. Gemiddelde operatietijd voor de robot-geassisteerde leverresecties was 160±78 minuten. Gemiddelde operatietijd voor de robot-geassisteerde pancreatoduodenectomieën was 420±67 minuten. Operatietijden van de robotprocedures bleven stabiel over de tijd en werden niet beïnvloed door de introductie van nieuwe chirurgen. Concluderend, stapsgewijze implementatie en uitbreiding van robot-geassisteerde HPB chirurgie is haalbaar en geassocieerd met goede klinische uitkomsten. Ondanks dat er nieuwe chirurgen werden geïntroduceerd in robot-geassisteerde HPB chirurgie bleven operatietijden, als indicator voor een leerproces, stabiel.

Hoofdstuk 10. Robot-geassisteerde pancreatoduodenectomie in een 10-jarig kind

Robot-geassisteerde pancreatoduodenectomie is mogelijk met name voordelig voor patiënten met een premaligne of benigne laesie, omdat deze patiënten een lange levensverwachting hebben en profiteren van de lange-termijn voordelen van de minimaal invasieve benadering zoals minder littekenbreuken, een kleiner risico op een strengileus en betere cosmetische resultaten. Deze video is een voorbeeld van een dergelijke casus. De patiënt is een 10 jaar oud meisje met een solide pseudopapillaire tumor, waarvoor een pancreatoduodenectomie was geïndiceerd. De verschillende stappen van de operatie zoals patiënt positionering, trocar plaatsing en de chirurgische stappen worden in deze video geïllustreerd.

Hoofdstuk 11. De eerste 100 robot-geassisteerde pancreatoduodenectomieën in Nederland

In dit hoofdstuk worden de resultaten van de eerste 100 pancreatoduodenectomieën in Nederland gepresenteerd. Data uit drie centra in Nederland (Erasmus MC, Maasstad Ziekenhuis, UMC Utrecht) werden verzameld uit prospectief bijgehouden databases en *post hoc* geanalyseerd. Resultaten van deze eerste 100 procedures in Nederland zijn veelbelovend: er waren slechts 22 patiënten (22%) met een ernstige complicatie, negentien patiënten (19%) met een pancreasfistel (ISGPS gr. B/C), negen patiënten (9%) met een postpancreatectomie bloeding (ISGPS gr. B/C), twee patiënten (2%) met nieuw-ontstaan multiorgaanfalen en geen postoperatieve sterfte. Om deze resultaten in perspectief te plaatsen, hebben wij aanvullend een systematisch literatuuronderzoek gedaan naar grote (> 500 procedures), recent gepubliceerde (afgelopen 5 jaar), cohort studies over open pancreatoduodenectomieën. Wij includeerden veertien studies die gezamenlijk de resultaten bevatten van 12.708 open pancreatoduodenectomieën. In deze veertien studies was de gepoolde mortaliteit 3%, de gepoolde morbiditeit 38%, kreeg 15% van de patiënten een postoperatieve pancreasfistel en trad er bij 7% een ernstige postpancreatectomie bloeding op. De resultaten van deze meta-analyse toonden aan dat de resultaten van de eerste 100 robot-geassisteerde pancreatoduodenectomieën in Nederland vergelijkbaar zijn met de uitkomsten van open pancreatoduodenectomieën.

Hoofdstuk 12 Robot-geassisteerde versus laparoscopische distale pancreatectomie

Conventionele laparoscopie lijkt een veilige en haalbare techniek voor distale pancreatectomieën. Desondanks worden er inmiddels ook distale pancreatectomieën middels robotchirurgie uitgevoerd, ondanks dat de voordelen van de operatierobot mogelijk minder evident zijn bij deze procedure. De optimale chirurgische precisie van de operatierobot heeft wel mogelijk enkele oncologische voordelen bij deze procedure, zoals meer R0 resecties en een toegenomen aantal gereseceerde lymfeklieren. In dit hoofdstuk hebben we de korte- en lange termijn oncologische uitkomsten vergeleken van patiënten die een robot-geassisteerde of laparoscopische distale pancreatectomie ondergingen vanwege een pancreas adenocarcinoom in Amerika tussen 2010 en 2013. Data werden verzameld uit de *National Cancer Database*. In totaal waren er 704 patiënten die een minimaal invasieve distale pancreatectomie ondergingen in die tijdsperiode, 605 (86%) patiënten middels conventionele laparoscopie en 99 (14%) patiënten middels robotchirurgie. Er was geen verschil in het aantal R1 resecties tussen de twee groepen (laparoscopie: 15% versus robotchirurgie: 16%, $p = 0.84$) en het aantal lymfeklieren in het resectiepreparaat (laparoscopie: 12 versus robotchirurgie: 11, $p = 0.67$). Ook de overleving verschilde niet tussen beide groepen (laparoscopie: 28 maanden versus robotchirurgie: 25 maanden, $p = 0.71$, HR: 1.1, 95% BI: 0.7-1.7). In de laparoscopie groep was het percentage conversies naar laparotomie wel significant hoger dan in de robot groep: 27% vs. 10%, $p < 0.001$.

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Book Chapter

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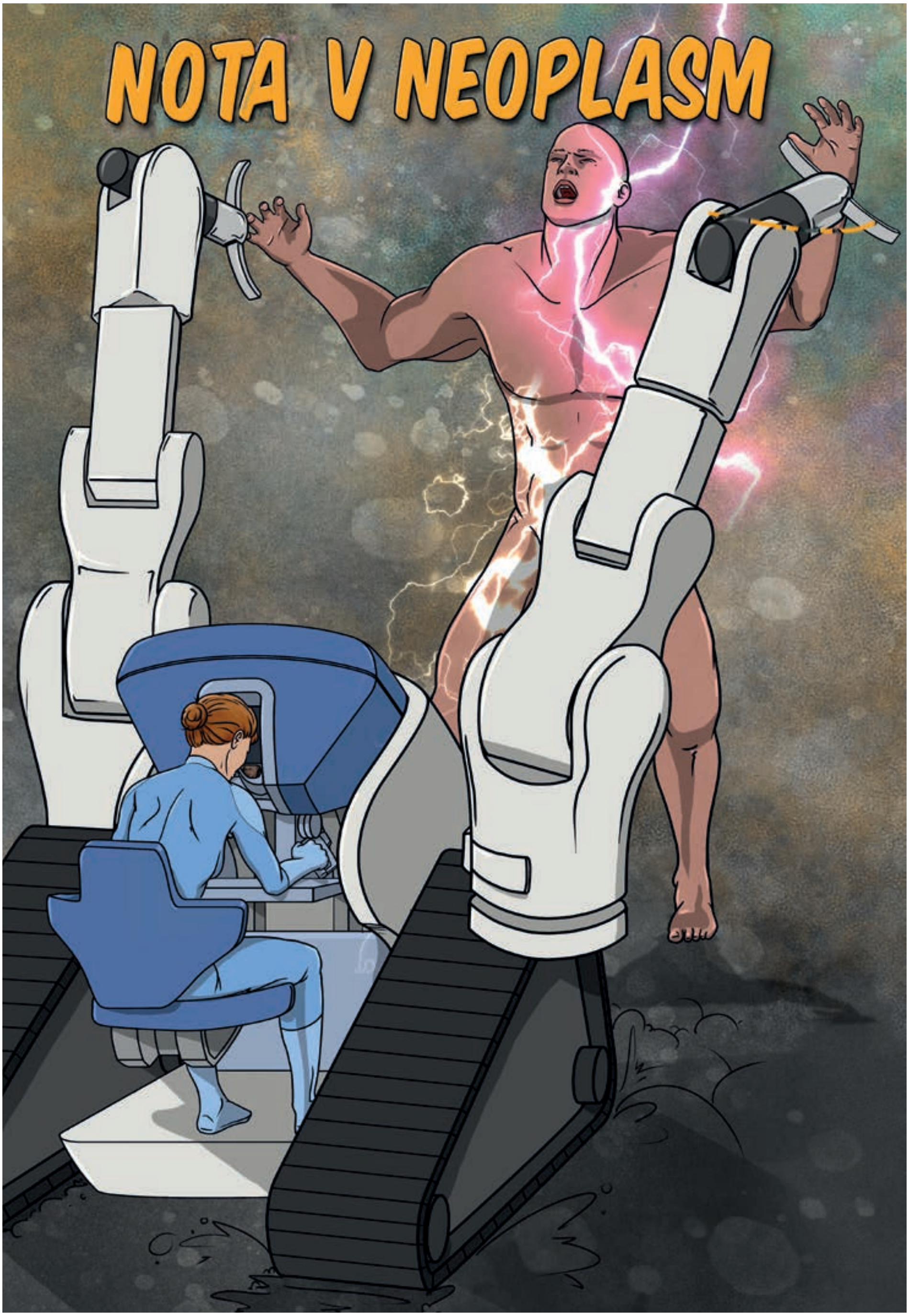

Nota versus Neoplasm. © Yuman Fong, 2019

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Curriculum vitae auctoris

Carolijn Nota was born on March 8th 1993 in Nijmegen, the Netherlands. After graduating from the Stedelijk Gymnasium Nijmegen in 2011, she started Medical School at Utrecht University in September 2011. In Utrecht, she was an active member of several student organizations. During her third year of Medical School she started participating in several research projects on robotic liver and pancreatic surgery at the Department of Surgery of the UMC Utrecht under supervision of dr. J. Hagendoorn, prof. dr. I.H.M. Borel Rinkes and prof. dr. I.Q. Molenaar. After doing research alongside her clinical rotations for several years, she moved to Los Angeles (California, USA) to do a research fellowship on robotic HPB surgery under supervision of prof. dr. Y. Fong and dr. Y. Woo at the Department of Surgery at City of Hope Comprehensive Cancer Center. Carolijn has received several grants for the research presented in this thesis, among others from '*Prof. Michael-van Vloten Fonds'*, '*Stichting Nijbakker-Morra*' and '*Stichting Jo Kolk Studiefonds'*. She presented her research at various national and international conferences, receiving several awards. After returning to the Netherlands, she graduated from Medical School in February 2019 and has spent the following summer completing her PhD thesis.

Currently, Carolijn lives in Utrecht and has started working as a resident not in training at the Department of Surgery of the St. Antonius Hospital in Nieuwegein (November 2019).