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REVIEW

Highlights, limitations and future challenges of laparoscopic resection for colorectal liver metastases

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HIGHLIGHTS

- The main obstacles to laparoscopic liver resection (LLR) for colo-rectal metastases (CRLM) are the risk of gas embolism, the difficulties to locate intraparenchymal lesions and to achieve hemostasis.
- LLR is associated with reduced blood loss, lower morbidity rates, shorter length of hospital stay and earlier return to functional activities.
- Other advantages of LLR could include less tissue damage, less surgical stress, and reduced overall costs.
- Oncological outcomes of LLR for CRLM such as rates of R0 margin and tumor recurrence, and 5-year overall survival offered by the laparoscopic approach seem similar to that obtained after open approach.
- However, the level of scientific evidence of comparative studies between open and laparoscopic approaches remains low, suggesting the need for further studies, including randomized control trials.

KEYWORDS
Laparoscopic liver resection;
Colorectal liver metastases;
Open approach;
Postoperative outcomes;
Survival

Summary The liver is the most common site for metastatic colorectal cancer (CRLM). Despite advances in oncologic treatment, resection of metastases is still the only curative option. Although laparoscopic surgery for primary colorectal cancer is well documented and widely used, laparoscopic surgery for liver metastases has developed more slowly. However, in spite of some difficulties, laparoscopic approach demonstrated strong advantages including minimal parietal damage, decreased morbidity (reduced blood loss and need for transfusion, fewer pulmonary complications), and simplification of subsequent iterative hepatectomy. Up to now, more than 9 000 laparoscopic procedures have been reported worldwide and long-term results in colorectal liver metastases seem comparable to the open approach. Only one recent randomized controlled trial has compared the laparoscopic and the open approach. The purpose of the present update was to identify the barriers limiting widespread acceptance of laparoscopic approach, the benefits and the limits of laparoscopic hepatectomies in CRLM.

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Introduction

Colorectal cancer is the third most common cancer and the third leading cause of cancer deaths in Western countries [1]. In France, 45,000 new patients develop colorectal cancer every year. The liver is the most common organ targeted by colorectal cancer metastases (CRLM), representing almost 50% of metastases. Approximately, 15—25% of colorectal cancer patients have synchronous CRLM at initial workup, and 20—30% patients developed subsequent liver metastases within few years following diagnosis [2].

Despite huge advances in chemotherapy and targeted therapy for colorectal cancer, liver resection is still the only potential curative treatment for patients with CRLM whereas advances in surgical techniques and perioperative care have decreased the 30-day mortality of liver surgery from 24% in 1970 to less than 2% presently [3]. A large number of studies reported that hepatic resection for CRLM provided favorable long-term survival, with 5 year and 10 year survival rates ranging from 33 to 58% and 23 to 39%, respectively [4,5]. In addition, a worldwide survey indicated that the long-term survival of patients with CRLM who underwent one to four liver resections due to hepatic recurrence was almost similar [6].

Although laparoscopic surgery for colorectal cancer has been largely evaluated and widely used [7], laparoscopic liver resection (LLR) has developed more slowly than other fields of laparoscopic surgery [8]. The purpose of the present update was to identify factors limiting widespread acceptance of laparoscopic approach, and to underline benefits and limits of LLR, together with the oncological relevance of LLR in CRLM.

Widespread acceptance of laparoscopic approach

Diffusion of laparoscopic approach in abdominal surgery

Historically, open surgery through laparotomy was the standard approach for abdominal procedures. Laparoscopy is a mini-invasive approach that allows performing abdominal procedures through small incisions with the help of a camera. Initially developed during the late 1980s for cholecystectomy, laparoscopy was progressively adopted for various abdominal oncologic and functional procedures during the last three decades. In this setting, a significant number of well-conducted randomized trials have demonstrated that the laparoscopic approach was associated with improved postoperative outcomes in various upper and lower gastrointestinal procedures including colorectal resections and esophageal resections without jeopardizing the oncologic outcomes of the patients.

Diffusion of laparoscopic approach in liver surgery

The first successful laparoscopic liver resection was reported in 1993, but the diffusion of laparoscopy in liver surgery has long been limited due to initial technical limitations (absence of specific laparoscopic devices for liver surgery), concerns regarding the safety of the patients (risk of gaz embolism or uncontrollable hemorrhage), doubts on the oncologic safety of the approach (risk of incomplete resection in segments of difficult access) and a long learning curve (since an expertise in both liver and laparoscopic surgery is needed). Hence, it is only in the early-mid 2000s that first large series reporting the safety and feasibility of laparoscopic liver resection were released. According to the French Registry, 5300 hepatectomies were performed in 2005 and it increased to 7800 in 2006, with a significant increase of ''atypical'' resections (1500 atypical resections in 2005 compared to 3500 atypical resections in 2006). Among these liver resections, the number of LLR increased from 550 in 2005 to 1100 in 2006 (respectively 10% and 16% of all hepatectomies) [9].

Limits of laparoscopic approach in liver surgery

Indeed, the laparoscopic approach of the liver does not allow the same access to the liver as the open approach, the anterior segments being easier to access to. Thus, some elementary open approach gestures such as liver palpation and mobilization, or vascular control and parenchymal transection may be challenging for an unexperimented laparoscopic liver surgeon. Vigano et al. suggested that a threshold of 60 cases was necessary in the learning curve for both minor and major LLR [10]. More specifically to CRLM, the fear of both involved resection margins and tumor dissemination at the trocar sites with a potential influence of the pneumoperitoneum have been initially reported by several authors [11]. However, many series challenged this assumption and this rare situation was described only in case of massive tumor spillage [8,12]. These different factors may have limited the development of the laparoscopic approach in the treatment of CRLM.

However, the development of new techniques and dedicated instruments has gradually allowed the diffusion of laparoscopic approach [13] and to date, more than 9000 laparoscopic liver resections have been performed and both feasibility and safety of this approach are now largely accepted [8].

Difficulty of laparoscopic liver resection

Some cases of LLR are widely accepted to be simpler, whereas others are more technically demanding [14,15]. Therefore, it was necessary to gradually increase skills of LLR according to the experience level before performing technically demanding procedures. For a safe diffusion of LLR, a clear training pathway was needed based on the assessed difficulty of particular procedures within the broad spectrum of LLR. However, whatever the surgical approach, the difficulty of a surgical procedure is hardly assessed, because its definition is subjective. A recent study by Ban et al. has attempted to assess surgical difficulty of LLR through a score using multiple variables such as tumor location, tumor size, proximity to the major vessels, or liver function [16]. Even though this scoring system can be used in the preoperative period, it remains complex to integrate all these variables in an objective prediction of technical difficulty.

In 2017, the group of the Institut Mutualiste Montsouris proposed a new classification to stratify the difficulty of LLR based on objective intraoperative variables including operative time, blood loss, and conversion rate [17]. In this stratification of LLR difficulty, Group I represents the first level and includes wedge resection and left lateral sectionectomy. Group II represents the intermediate level with anterolateral segmentectomy and left hepatectomy. Last, Group III represents the highly advanced level including posterosuperior segmentectomy, right posterior sectionectomy, right hepatectomy, extended right hepatectomy, central hepatectomy, and extended left hepatectomy. Procedures in Group I should not be considered as ''easy'', but less technically demanding and less difficult than other LLR. Thus, Group I procedures should be suitable for liver surgeons at the beginning level of LLR. This classification was expected to serve as a guide determining whether laparoscopic approach can be used, depending on the surgeons' technical levels. In addition, it can be helpful for reducing the potential risk caused by technically demanding LLR procedures that are beyond the surgeons' technical levels.

Benefits of laparoscopic liver resection in CRLM

Several studies has highlighted the added values of LLR versus open liver resection (OLR) in terms of reduced blood loss, lower morbidity rate, shorter length of hospital stay and earlier return to functional activities [18—24]. Moreover, other advantages including less tissue damage, surgical stress, and overall costs have also been reported [25,26]. Two randomized controlled trials comparing open and laparoscopic approaches in liver resection have been conducted. Unfortunately, the first one (Orange II, NCT00874224) was stopped after failing to recruit patients [27]. The second one ''Oslo CoMet trial (NCT01516710)'' was completed ($n = 280$) and demonstrated a significantly lower 30-day complication rate in the laparoscopic-surgery group compared to the open-surgery group [19% vs. 31%) [12]. However, only patients undergoing minor resection for less than 4 lesions were selected and no survival analysis was performed. Short-term outcome results of comparative series of laparoscopic versus open resections of CRLM are detailed in Table 1. Interestingly, in the study of Vanounou et al., the economic impact of the laparoscopic approach was noteworthy, with the laparoscopic approach US$1527—2939 more cost efficient per patient compared to the open technique [26].

A theoretical advantage for LLR is reduced blood loss due to the increased intra-abdominal pressure due to pneumoperitoneum, thus counteracting venous bleeding from the liver [40]. This difference in blood loss and transfusion requirement may be related to the magnified images allowing a more meticulous dissection, and a decreased blood loss from the abdominal wall provided by laparoscopic approach [41]. Indeed, the hemostatic effect of the intra-abdominal pressure induced by the pneumoperitoneum and the magnified view in laparoscopy may allow surgeons precise identification and management of vasculobiliary structures [42]. However, while most of retrospective series reported a benefit of laparoscopic approach on blood loss, the first and only randomized controlled trial published about LLR versus OLR of CRLM did not observe a significant difference regarding the intraoperative blood loss and showed a similar rate of transfusion (8%) in both arms [12]. In a recent series, Tomimaru et al. reported the first series questioning the validity of intraoperative blood loss measurement through suction of the blood accumulated in the abdominal cavity [43]. The authors stated that due to a reduced workspace, blood suction might be less efficient in LLR compared with OLR, leading to an underestimation of intraoperative blood loss and highlighting the notion of ''hidden blood loss''. Of course, the importance of these results does not question the benefit of the laparoscopic approach since several significant limitations such as population heterogeneity, limited sample size, study reproducibility of the blood measurement, limit the strength of the message. However, it raises the question of reconsidering blood loss analysis during liver resection. Nevertheless, it should be kept in mind that impact of intraoperative blood loss on the postoperative outcomes is more relevant than the precise blood loss volume. In a recent series, an increased estimated blood loss > 250 ml was associated with significantly higher overall complications and mortality after LLR [44]. In other words, bleeding repercussions might therefore be best illustrated by blood transfusion requirement instead of intraoperative blood loss volume. Anyway, further trials focusing more specifically on blood loss measurements will provide additional data clarifying the benefit of laparoscopic approach on blood loss.

Moreover, several studies have demonstrated that patients might benefit from laparoscopic surgery with lower morbidity in many other abdominal surgeries [45,46]. After liver surgery, postoperative pulmonary complications are as common as cardiac complications and have yet been reported to greatly contribute to death and complication following surgery [47,48]. Several factors are known to contribute to the occurrence of postoperative pulmonary complications in liver surgery. Of these a history of diabetes mellitus, a transverse subcostal bilateral muscle-cutting incision, a prolonged surgery, the presence of a nasogastric tube, and the need for intraoperative blood transfusion, are more strongly associated with their development [47]. Open major hepatectomies are mostly performed through bilateral subcostal or J-shaped incisions, with transection of the abdominal oblique and rectus muscles and prolonged retraction of the right hemi-diaphragm. On one hand, these large incisions may increase the risk of postoperative pulmonary complications through several mechanisms, including painful limitation of the rib cage excursion but also modification of diaphragmatic lymphatic drainage following dissection in the vicinity of the diaphragm and the diaphragmatic peritoneum. Open approach may result in a 50-60% reduction of the vital capacity and a 30% reduction in functional residual capacity [47]. On the other hand, although pneumoperitoneum increases pulmonary resistance, which can in turn result into intraoperative hypercapnia and negatively affect the postoperative pulmonary recovery [48], the laparoscopic approach resulted in a dramatically decreased surgical wall trauma since only 5 or 6 port incisions are needed and the resected specimen is extracted through limited incisions including a suprapubic one without muscle section in 65% of the cases. In this context, decreased postoperative pain and early postoperative rehabilitation [49] may therefore provide improved pulmonary function recovery.

Finally, in addition to its clinical feasibility and safety, the cost-effectiveness of LLR was extensively debated, due to the expensive upfront payments for the disposable laparoscopy-related devices. Indeed, the benefit of LLR in term of cost-effectiveness may be attributed to the reduced postoperative morbidity rate, and shorter hospital stay [26]. In a US nationwide inpatient sample including 21280 patients who underwent liver resection from 2002 to 2012, the laparoscopic approach was consistently associated with improved postoperative outcomes including decreased postoperative morbidity (OLR vs. LLR: 32.9 vs. 29.6%) and a shorter length of hospital stay (≤ 4 days; LLR, 21.4%; OLR, 13.7%; both $P < 0.05$) [50]. Thus, it seems possible to

Table 1 Results of comparative series of laparoscopic resection of cancer colorectal liver metastases: short- and long-term outcomes.

Author	Study period	Country	Design	Group	*n*	Operative time	Blood loss	Major resection	Conversion rate	Morbidity	Mortality	Length of stay	R0 margins	3/5 year OS	3/5 year DFS
Mala et al., 2002 [28]	1998—2001	Norway	Comparative	Open	18	185	500	0%	—	29%	0%	8.5 days	89%	NA/NA	NA/NA
				Lap	21	187	600	0%	0%	13%	0%	4.0 days	95%	NA/NA	NA/NA
Castaing et al., 2009 [18]	1997—2007	France	Case-control	Open	60	294	NA	38%	—	28%	1.7%	11.0 days	72%	70%/56%	40%/27%
				Lap	60	278	NA	40%	10%	27%	1.7%	10.0 days	87%	82%/64%	47%/35%
Topal et al., 2012 [24]	2002—2008	Belgium	Case-control	Open	20	232	550	65%	—	35%	0%	8.0 days	95%	NA/NA	NA/NA
				Lap	20	257	550	85%	NA	35%	0%	8.0 days	95%	NA/48%	NA/43%
Cannon et al., 2012 [4]	1995—2010	USA	Comparative	Open	140	NA	392	51%	—	50%	1.4%	8.3 days	86%	60%/37%	35%/22%
				Lap	35	NA	202	54%	NA	23%	0%	4.8 days	97%	63%/36%	37%/15%
Cheung et al., 2012 [29]	2002—2011	China	Case-control	Open	40	210	310	5%	—	5%	0%	7.0 days	NA/NA	NA/NA	NA/NA
				Lap	20	180	200	5%	10%	10%	0%	4.5 days	NA/NA	NA/NA	NA/NA
Guerron A et al., 2013 [30]	2006—2012	USA	Case-control	Open	40	219	376	22%	—	20%	NA	6.5 days	NA	81%/NA	40%/NA
				Lap	40	239	753	12%	5%	15%	NA	3.7 days	NA	83%/NA	38%/NA
Iwahashi et al., 2013 [31]	2007—2012	Japan	Case-control	Open	21	369	326	0%	—	24%	0%	27.0 days	NA	89%/51%	33%/25%
				Lap	21	377	198	5%	NA	10%	0%	18.3 days	NA	84%/42%	14%/14%
Montalti et al., 2014 [32]	2005—2012	Europa	Case-control	Open	57	288	691	23%	—	32%	0%	9.2 days	91%	75%/65%	42%/38%
				Lap	57	284	454	23%	16%	16%	0%	6.5 days	87%	75%/60%	39%/29%
Kubota et al., 2014 [33]	2006—2013	Japan	Comparative	Open	62	306	580	21%	—	9.7%	0%	14.2 days	94%	74%/NA	68%/NA
				Lap	43	333	287	7%	NA	2.4%	0%	7.3 days	100%	88%/NA	48%/NA
Tohme et al., 2015 [23]	2009—2013	USA	Case-control	Open	66	NA	250	23%	—	38%	0%	5.0 days	89%	60%/39%	NA/NA
				Lap	66	NA	150	23%	4%	26%	0%	4.0 days	88%	74%/51%	NA/NA
Untereiner et al., 2015 [34]	2012—2015	France	Case-control	Open	18	180	200	17%	—	44%	0%	6.5 days	94%	83%/NA	78%/NA
				Lap	18	230	30	11%	5.6%	17%	0%	6.0 days	94%	100%/NA	89%/NA

Table 1 (*Continued*)

Author	Study period	Country	Design	Group	*n*	Operative time	Blood loss	Major resection	Conversion rate	Morbidity	Mortality	Length of stay	R0 margins	3/5 year OS	3/5 year DFS
Hasegawa et al., 2015 [19]	1997–2013	Japan	Comparative	Open	69	277	620	36%	–	25%*	1.4%	16.0 days	91.3%	NA/49%	NA/29%
				Lap	102	228	127	19%	1%	9%*	0.9%	9.0 days	93.1%	NA/57%	NA/40%
Beppu et al., 201 [55]	2005–2010	Japan	Case-control	Open	342	277	415	6%	–	12.7%	0%	14.0 days	92.1%	81%/68%	54%/51%
				Lap	171	282	163	6%	NA	14.1%	0%	12.0 days	90.0%	84%/70%	55%/53%
Nachmany et al., 2015 [35]	2010–2015	Israel	Comparative	Open	132	241	422	38%	–	35%	0.7%	8.4 days	88.6%	72%/NA	NA/NA
				Lap	42	282	251	12%	11.9%	24%	0%	6.7 days	90.4%	64%/NA	NA/NA
Allard et al., 2015 [36]	2006–2013	France	Case-control	Open	153	NA	NA	43.7%	–	32.7%	3.9%	NA	82.8%	84%/75%	52%/36%
				Lap	153	NA	NA	45.8%	1.7%	12.4%	3.0%	NA	88.0%	88%/78%	40%/32%
Karagkounis et al., 2016 [20]	2006–2015	USA	Case-control	Open	65	210	300	6%	–	40%	0%	6.0 days	83.1%	75%/54%	NA/NA
				Lap	65	235	400	6%	7.7%	26%	0%	4.0 days	78.5%	76%/62%	NA/NA
Lewin et al., 2016 [37]	2000–2014	Australia	Case-control	Open	139	174	570	54%	–	27%	1.4%	7.8 days	82%	NA/63%	NA/38%
				Lap	147	132	300	42%	8.9%	17%	0%	5.0 days	91%	NA/54%	NA/36%
Cipriani et al., 2016 [38]	2004–2015	UK	Case-control	Open	133	210	500	54%	–	39.8%	1.5%	7.0 days	86.5%	69%/62%	36%/24%
				Lap	133	295	400	51%	9.8%	23.3%	0.8%	4.0 days	92.5%	77%/64%	30%/24%
Martinez-Cecillia et al., 2017 [39]	2005–2012	Europa	Case-control	Open	225	225	400	24%	–	39%	0%	8.0 days	88%	60%/46%	46%/29%
				Lap	225	230	250	21%	7.6%	22%	0%	5.0 days	88%	68%/43%	43%/31%
Fretland et al., 2018 [12]	2012–2016	Norway	RCT	Open	147	120	200	0%	–	31%	0.6%	4.0 days	71%	NA	NA
				Lap	133	123	300	0%	2.0%	19%	0%	2.2 days	71%	NA	NA

OS: Overall Survival; DFS: disease free survival; NA: not available.
* Major complications; RCT: randomized controlled trial.

hypothesize that LLR might provide economic benefit in patients with CRLM, based on a reduced morbidity and a shorter hospital stay.

Specificities of colorectal liver metastases

Parenchymal sparing liver resection

Parenchymal sparing liver resection has been developed in open surgery to preserve hepatic function while achieving sufficient surgical margins. An increasing number of series have highlighted both technical and oncological benefits of parenchymal sparing hepatectomy in comparison with major hepatectomy [51,52]. However, laparoscopic approach was not popular in parenchymal sparing hepatectomy for deeply located tumors because it was more technically demanding since manipulations are limited [14,53]. In laparoscopic approach, parenchymal sparing hepatectomy for deeply located tumors in difficult-to-access areas can require intricate curved transection planes, technically more difficult than a single and straight transection plane during major hepatectomy [17,54]. For these reasons, major hepatectomy resecting more non-tumorous parenchyma than required for tumor clearance, was often performed by laparoscopy. Recent technical advancement and better understanding of hepatic anatomy have enabled to perform laparoscopic parenchymal sparing hepatectomy even in difficult-to-access lesions [55] such as upper central [56] or posterosuperior segments [57], with a subsequent decrease of the rate of major hepatectomy. In these settings, surgeons should reconsider the importance of parenchymal sparing strategy and try to minimize the extent of resection even by laparoscopy.

Oncologic quality of the resection and long-term outcomes

Most series indicate that LLR allow similar oncological outcomes than OLR, such as tumor free surgical margins, 3- and 5-year disease-free and overall survival. Long-term outcome results of comparative series of laparoscopic versus open resections of CRLM are detailed in Table 1.

However, the positive results from LLR must be interpreted with caution due to the potential selection biases and small sample size, which may lead to inaccurate evaluation of outcomes and uncertain conclusions. The majority of relevant data were extracted merely from case series, case-control studies or meta-analyses of these studies [32,35]. The sample size from each trial ranged from 36 to 450, that might explain the inconsistencies across different trials and have influenced the level of the evidence from these studies [4,5,34,36,38,39,58,59]. Indeed, most of studies were completed between 1997 and 2016, and the huge advances in both chemotherapy and targeted therapies in the treatment of CRLM might explain the significant improvement of prognosis during this period. Therefore, the impact of the laparoscopic approach on the overall and disease-free survival after resection of CRLM is really difficult to identify. Also, the comparability of the patients included in these series is debated since the patients undergoing LLR of CRLM had smaller and more peripheral metastases than those treated with the open approach.

An interesting expected benefit of LLR in patients with CRLM would be its theoretical oncologic superiority. This could be achieved (i) provided that the oncologic quality of the resection (margins, rate of parenchymal sparing resection, quality of laparoscopic ultrasonography) is at least similar to that of OLR; and (ii) through a decrease of overall postoperative complications. Indeed, the long-term prognostic influence of major postoperative complications for different cancers (such as esophageal cancer) has previously been established and thus the observed improvement in survival from minimally invasive surgery, maybe mediated by the reduction in major complications.

In the specific setting of CRLM, decreasing postoperative complications yields two theoretical advantages: (a) a direct oncologic effect through a decrease in recurrence; (b) a higher feasibility of adjuvant chemotherapy including a shorter time to return to chemotherapy. The randomized study by Fretland et al. indicated that LLR was superior to open resection in reducing the inflammatory response [60]. This decreased inflammatory response is associated with better-preserved immune function during the postoperative period, which may lower the risk of surgical complications [61]. Hence, the reduced inflammatory response achieved by laparoscopic approach might be one of the explanations for the decreased morbidity observed in the different series.

Interestingly, a recent study using a propensity score matching, found an approximately 2 weeks benefit for adjuvant chemotherapy administration after LLR. More importantly, in this series, all patients started adjuvant chemotherapy within 8 weeks after LLR, unlike OLR patients who had delayed adjuvant chemotherapy start in 34% of cases [62]. The hypothesis is that, besides its potential impact on postoperative complications and the diminished surgical trauma, the minimally invasive approach may shorten postoperative recover, and thus help to start adjuvant chemotherapy within appropriate timing.

CRLM recurrence

Repeat hepatectomy for CRLM recurrence is increasingly performed owing to recent advances in the early diagnosis of recurrence, in chemotherapy efficiency, and in the expertise of hepatic surgery. In 2016 the group of the Institut Mutualiste Montsouris showed that laparoscopic repeat resection for recurrent CRLM was feasible and safe with acceptable perioperative mortality and morbidity after second and third LLR [63]. In addition, laparoscopic repeat hepatectomy provides an additional benefit of overall survival similar to that provided by first LLR. Even though laparoscopy significantly decreases adhesions formation, significant adhesions were observed in patients who had previous laparoscopic major hepatectomy or any other procedure in which the hepatic pedicle was dissected. A second or a third hepatectomy, even by laparoscopy, is technically more demanding and more time consuming due to technical difficulties from intra-abdominal adhesions, variations in liver anatomy on the hypertrophied remnant, chemotherapy induced liver injury but also higher intraoperative bleeding resulting in a higher risk of complications [64].

Bilobar disease and patient installation

In some situations, such as bilobar disease, laparoscopic resection of a posterior lesion associated with a lesion in left lobe for example can be difficult with a single installation of the patient. Indeed, for laparoscopic resection of lesions located in the posterior segment, the patient is placed in the left lateral decubitus position with the right arm suspended. In addition to 3 trocars placed in the right upper quadrant of the abdomen, 2 balloon-tipped trocars in order to isolate the chest from the abdominal cavity, one 5 mm and one 10 mm, can be disposed through the diaphragm in the same intercostal space. In this setting, the operative table should be rotated provided that reinforcement band prevent the patient fall. In some infrequent situations, the patient could be reinstalled during the surgical procedure in order to facilitate access to some « difficult segments ».

Laparoscopic ultrasonography

Ultrasound exploration of the liver during laparoscopic resection of CRLM is more challenging than in open approach especially when both posterior and anterior lesions need to be resected. Laparoscopic ultrasonography has been proven to be an indispensable tool in all laparoscopic liver procedures [65—67]. The laparoscopic ultrasonography allows all intraoperative procedures such as resection, biopsy, or radiofrequency ablation. The major disadvantage of laparoscopic ultrasonography is that the image orientation is difficult to interpret. The images are small, specular, and present with shadowing and reflection artifacts with a variable contrast. Therefore, the quality of the image is operator-dependent, which represents another disadvantage. Nevertheless, the real-time imaging capabilities and the convenience of laparoscopic ultrasonography for intraoperative use compensate many of the disadvantages. Indeed, development of navigation technology or the use of contrast agents during laparoscopic procedures guided by laparoscopic ultrasonography would solve the orientation problems in the future.

Future advances

Augmented reality guidance systems

Despite its proven benefits and the adaption of modern technology to reduce the learning curve, minimally invasive liver surgery is presently used only in specialized centers. Surgeons still struggle with the anatomy and identification of major vascular and nonvascular structures within the liver parenchyma. Although preoperative CT and intraoperative ultrasonography are useful to surgeons, these imaging systems are either not in real-time or they show only a small part of the entire picture. As a result, many researchers are working on developing a real-time anatomical map of a patient's liver to assist surgeons navigate challenging dissections. Augmented reality guidance systems have been used for real-time image guidance. Surgeons can obtain intraoperative fluoroscopic C-arm con-beam CT (CBCT) images. Software can be used to produce a real-time overlay of these images to highlight important structures during dissection. Ideally, if augmented reality guidance systems can provide real anatomical information during surgery, it can help orient surgeons, which would lead to fewer intraoperative complications [68].

ICG is a widely available dye that absorbs and emits light in the near-infrared (NIR) spectrum. Advances in imaging technologies have led to the development of NIR cameras to visualize injected dye in humans. Because ICG is hepatically cleared, it has become clinically important in liver surgery because it can identify intrahepatic lesions even when preoperative CT, palpation, inspection, and intraoperative ultrasound cannot [69]. Well-differentiated tumors absorb ICG, therefore result in homogenous fluorescence. Poorly differentiated and metastatic tumors do not absorb or excrete dye therefore develop a rim of ICG or halo sign [70]. In a study published in 2014, 276 hepatocellular carcinomas were resected, including 273 identified by ICG (99% success rate) [71]. In a series of 40 patients with CRLM, intraoperative ICG discovered unanticipated LM in 5 (12,5%) [71]. ICG can even be used to distinguish benign from malignant lesions [69]. Use of this dye has been used to increase identification of lesions and is being more frequently employed for both open and minimally invasive approaches.

3D Visualization

Three-dimensional (3D) visualization gives better depth perception than the tradition two-dimensional (2D) screens used in laparoscopy. This enhanced depth perception is excellent to enable accurate dissection and identification of intraparenchymal vessels. A study by Velayutham et al. compared major liver resection using 3D and 2D laparoscopy. No difference was seen in blood loss or major complications; however, the operative time was significantly shortened in the 3D group [72].

Robotic Instruments

Ergonomics is still a problem for complex laparoscopic surgery. There is a limited number of degrees of freedom (DOF) of laparoscopic instruments due to the passage of the shaft through the trocar as well as the fixed position of the trocar on the abdominal wall. These factors limit laparoscopic instruments to four DOF compared to a human arm, which has nine DOF. As a result, this limits the surgeon's freedoms of movement including during the most basic surgical maneuvers like tying intracorporeal knots. As a result, most of laparoscopic surgeons suffer from musculoskeletal pain often in the upper back and neck due to awkward positioning while performing surgery [73]. To overcome these two issues, researchers are developing robotized laparoscopic instruments, to improve surgeon postures and add more DOF thus facilitating the most difficult surgical maneuvers [74,75]. In addition, these instruments allow the surgeon to still receive haptic feedback, that telemanipulated surgical devices like the da Vinci® robot cannot provide [76]. These new robotized instruments appear to be the future of laparoscopic surgery since they improve ergonomics and surgical skill, and could increase the overall quality of the surgical procedure.

Conclusion

Although laparoscopic surgery for primary colorectal cancer is well documented and widely used, laparoscopic surgery for CRLM has developed more slowly. The presumed obstacles to this approach included foremost a long-lasting learning curve, fear of difficult-to-control bleeding or gas embolism, and issues regarding patient selection. However, in spite of these difficulties, laparoscopic approach showed strong advantages in early postoperative course, and offered similar oncological outcomes compared with open approach. A large pragmatic randomized study with less selection of the patients could reinforce its diffusion in the field surgery of CRLM.

Insert here the HIGHLIGHTS (see attached file)Disclosure of interest

The authors did not declare their eventual competing The authors have not supplied their declaration of competing interest interests.

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