Review

Surgical treatment of liver metastases of colorectal cancer: Strategies and controversies in 2006

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Abstract

Aims: To review the latest strategies and controversies in the surgical treatment of liver metastases of colorectal cancer systemically and comprehensively.

Methods: A medline based literature search on relevant topics was performed in PubMed for key articles concerning the novel strategies and controversies in the management of liver metastases of colorectal cancer. Some information was obtained from ‘Proc Am Soc Clin Oncol’ published recently. The findings and discussions were related to our own experiences.

Results: Although for well-indicated patients, a consensus has been reached that hepatic resection is the only management that could provide the patients curability, there still exist many controversies, such as the prognostic evaluation, contraindications to hepatic resection, treatment for synchronous liver metastases, the place of laparoscopic surgery, etc. Meanwhile, various strategies to improve the respectabilities are available, including neoadjuvant chemotherapy, portal vein embolization, two stage hepatectomy, and some locally ablative approaches. The current condition is difficult and sometimes confusing for a relevant surgeon when designing treatment protocols for more complex diseases.

Conclusion: As the advancing of the management of liver metastases of colorectal cancer, more patients will become candidates for and benefit from potentially curative surgical resections. Optimal effect could only be achieved when used in a manner tailored to the individual patient.

Keywords: Colorectal cancer; Liver metastases; Liver resection; Prognosis

Introduction

Hepatectomy is currently considered to be the standard of care, and remains the only potentially curative therapy for liver metastases of colorectal cancer (LMCC). Complete surgical resection of isolated or multiple hepatic metastases has been associated with a 26–51% 5-year survival and confers an obvious survival advantage compared to patients not undergoing resection.1–5 Five-year survivors using chemotherapy alone are anecdotal. Advances in surgical technique and relevant strategies, such as neoadjuvant chemotherapy, portal vein embolization, and a planned two-stage hepatectomy, have increased the number of potential candidates for liver resection. However, despite the advances in the knowledge and treatment modalities of LMCC, at most 20% of patients could be candidates for potentially curative resection at present.6–8 In this review, we will assimilate the information on the latest strategies and controversies in the management of LMCC.

Natural history

The knowledge of the natural history of LMCC is a must in understanding the benefit of medical/surgical interventions. The outcome of untreated hepatic metastases is usually dismal, with a median survival of 6–12 months,9–11 though there have been limited case reports describing a slow evolution form of LMCC.12 Chemotherapy alone, whether delivered systemically or regionally, rarely results in a prolonged survival and is generally considered palliative. Although there were no randomized trials comparing the resection, chemotherapy and best supportive care in patients advanced...
Recent advances in prognostic evaluation

Although complete surgical resection could be curative for some patients, the majority of patients will eventually develop recurrent disease after surgery. Furthermore, as many as 20% of patients will be found metastatic disease within 6 months of resection. Apparently, a clearly defined and widely applicable prognostic scoring system based on clinical parameters would be of great help, either for optimizing the patient selection or for stratification of patients in relevant clinical trials. Almost 10 years ago, Nordlinger and colleagues from a French Multicenter Study introduced the first scoring system for patients with LMCC, based on the data from 1568 patients who accepted potentially curative resections. In this largest series available, they identified three groups of patients with low, intermediate and high risk for poor prognosis based on seven high risk factors. Since then, at least six more scoring systems have been developed, among which Fong and colleagues’ proposal attracted more attention for being the largest single-institution experience. They proposed a clinical pre-operative risk scoring system based on outcomes of 1001 patients undergoing liver resection for LMCC in Memorial Sloan-Kettering Cancer Center between 1985 and 1998. Five clinical parameters were selected, including primary nodal status, disease-free interval from the primary to liver metastases of <12 months, number of hepatic tumours >1, pre-operative CEA level >200 ng/ml, and size of the largest hepatic tumour >5 cm, as criteria for a clinical risk score. Each criterion was assigned one point. They found that the total score was highly predictive of long-term outcome. The 5-year survival for patients with zero points was 60%, whereas for those with five points was 14%. Age, gender and type of resection do not seem to influence the prognosis. However, if the margin status and the presence of extrahepatic lesions in their system, because they thought that these two were clearly the most influential factors if they were positive and should be considered as contraindications for liver resection.

Along with the dramatic changes in the treatment of LMCC, the concept as to prognostic factors is also changing. Some generally accepted negative prognostic factors have lost their places, while some other new ones appear as substitutes. For example, Wanebo et al. found that patients with three or more metastases had a significantly poorer disease-free survival than those with a single or two metastases. So they advocated that the presence of four or more liver lesions should be taken as a contraindication to resection, even when technically feasible. But recent reevaluations of the impact of the number of metastases on prognosis after liver resection have revealed the potential benefit in patients with four or more metastatic lesions. Minagawa et al. reported the Japanese experience that among the 235 patients who underwent liver resection for metastatic colorectal cancer, including 53 (22.6%) with ≥4 lesions, the actual 10-year life expectancy of patients with four or more metastases was 29%, which was almost equivalent to the long-term survival of patients with only one solitary metastasis. Now it has been generally accepted that the number and size of metastases do not contribute much to prognosis, if satisfactory resection could be achieved technically and anatomically. Recently, Adam et al. reported that tumour progression while on modern chemotherapy is strongly associated with a poor outcome after liver resection, even if the surgery itself is potentially curative. Hence, the tumour response to neoadjuvant chemotherapy might be a novel prognostic factor for LMCC patients after hepatic resection.

Recent advances in contraindications to hepatic resections

The importance of prognostic factors lies in two aspects, i.e. prognosis evaluation and surgical candidates selection. Very strong negative prognostic factors might become absolute or relative contraindications. As we have stated, the pattern of prognostic factors is evolving in conjunction with the advances in the treatment of LMCC and the accumulation of relevant knowledge. So are the contraindications to hepatic resections for LMCC. Many factors have been described in numerous reports, among which three have been consistently and discriminatorily considered to be the absolute or relative contraindications to the hepatectomy, i.e. the presence of extrahepatic disease (EHD), involvement of hepatic pedicle lymph node (HP-LN) and an inadequate resection margin of <1 cm. In some recent studies, all three factors have been greatly challenged and might lose their importance in patient selection for hepatectomy.

Lately Elias and colleagues reported a series of 84 patients over a period of 13 years, who underwent complete resections of EHD (sites of metastases including lung, ovary and hepatic lymph nodes) simultaneously with hepatic resection. The overall 5-year survival was 28% as compared with 34% in the 224 patients undergoing hepatectomy without EHD during the same period of time. What’s more, their study also demonstrated that the total number of metastatic lesions has a stronger negative prognostic value after complete resection of the metastases, compared with the location.

In one prospective study reported recently by Jaeck et al., the traditional status of HP-LN involvement in the treatment of LMCC was challenged. Distinctively different from all
the previously published reports, they categorized the HP-LN into two groups, which showed distinct prognostic significance for LMCC after hepatectomy and relevant lymphadenectomy. The survival rate in patients with positive HP-LN was significantly lower than in the negative group (3-year survival 19 vs 62%, \( P < .0001 \)), however, those with the involvement of lymph nodes limited to the hepatoduodenal ligament and retropancreatic portion demonstrated a much superior prognosis to those that the lymph nodes around the common hepatic artery and celiac axis were involved after the R0 resections (3-year survival 38 vs 0%, \( P < .001 \)).

Another factor traditionally considered to be an absolute or relative contraindication to hepatic resection in LMCC is the predicted resection margin of \(< 1 \text{ cm}.^{26-28} \) Compared with the other two contraindications above mentioned, there are far more reports challenging its status for prognosis evaluation and the adequacy as a contraindication in surgical patients selection. Elias et al. reported a prospective study, in which 136 out of 196 patients had resection margins of less than 1 cm. The overall 5-year survival in these 136 patients was 27.8%, which is comparable to those with resection margins more than 1 cm. Recently Pawlik et al. published a multicenter report of 557 patients undergoing hepatic resection for LMCC over a period of 14 years, including 45 positive margins, 214 margins of \(< 1 \text{ cm} \) and 298 margins of \( \geq 1 \text{ cm} \).\(^{31} \) The 5-year survival was 63.8% for all the patients of negative margins, but no significant survival difference could be demonstrated between groups of different extent of margins. Even in the patients with microscopically positive margins, the 5-year survival could be as high as 17.1%.

Taken together, all the three once-considered absolute or relative contraindications have met great challenges, although further large, prospective, randomized and well-controlled trials are highly needed to confirm the findings. It is fair to state that some negative prognostic factors and contraindications, even if being very potent currently, could probably fade in their importance as our experience accumulate. Accordingly it is important to stress that the current discussion on prognostic factors and contraindications is at a stage as it was for colorectal secondaries some 20 years ago. Current clinical prognostic factors might be used to predict outcome, but not to exclude patients from surgeries. At present, the only generally accepted contraindication to hepatectomy is the impossibility to remove all the lesions while leaving sufficient functional hepatic parenchyma, regardless of the location, distribution, number or size of the metastases. It is rational to anticipate that as more and more modalities available to improve the technically unresectabilities, together with the amelioration of prognostic considerations, the number of patients with colorectal liver metastases suitable for hepatectomy will increase.

### Pre-operative considerations

#### Fine needle aspiration

Fine needle aspiration (FNA) cytology is a well-established approach for histological diagnoses of liver tumours. Its adverse effects have long been greatly underestimated. For example, the seeding along the needle tract has been believed to be very rare, with an incidence of 0.003–0.07%. Recently, much higher incidences of needle tract metastases have been reported (10–19%).\(^{34-36} \) Furthermore, it has been demonstrated that pre-operative FNA in patients with LMCC confers poorer long-term survival of LMCC after hepatic resection compared to patients without FNA.\(^{34} \) The potential benefit of FNA in suspected patients is the cytological confirmation of suspected metastases, and this might be obtained effectively by other examinations together with the history, since the possibility of benign lesions to be misdiagnosed as metastases is very low. On the other hand, the benefit will be outweighed by the risk of the serious and often fatal complication of needle track deposits and also the risk of deriving false reassurance from a false negative result. So in view of the up-dated data, we strongly recommend that potentially resectable LMCC be diagnosed and treated without FNA.

#### Pre-operative evaluations

Pre-operative evaluations for potential candidates of hepatic resection for colorectal metastases are aimed at making an overall assessment of their underlying medical condition, determining the extent of extrahepatic disease, and evaluating the resectability of liver metastases.

Operative risk assessment is similar to other major abdominal procedures, but particular attention should be directed to pulmonary and cardiac complications. Measurement of hepatic parenchymal function is not routinely indicated, unless the patient has underlying liver disease. The presence of hepatomegaly, ascites, or jaundice should raise the suspicion of massive replacement of liver parenchyma by tumour or the concomitant liver disease.

Radiology staging is vital to determine the suitability of partial hepatectomy. The goal of diagnostic imaging is to define the extent of lesions both intrahepatically and extrahepatically. Generally, the often-used and valuable imaging modalities include ultrasonography, CT scan and MRI. In expert hands, they are all very useful to define the number and size of lesions, as well as their relationship to major blood vessels. The use of PET to help making more precise evaluation to avoid unnecessary laparotomy has been reported, but large, prospective studies still needed to substantiate the results.\(^{37-40} \) As to PET/CT, a recently published prospective study demonstrated similar value to contrast-enhanced CT when used in LMCC.\(^{41} \)
In recent years, the advancing of minimal invasive surgery has led to increasing use of laparoscopy for evaluating LMCC patients pre-operatively, so as to spare them the risk and discomfort of an exploratory laparotomy. This procedure has been reported to be able to exclude 25–48% of patients from exploratory laparotomy, and the false negative rate of the procedure is less than 15%. Now it has been widely accepted that pre-operative laparoscopy could avoid the unnecessary laparotomy in approximately 1/3 of patients deemed resectable by pre-operative evaluation.

Surgical resection

A detailed discussion of the techniques of liver resection is beyond the scope of this review, but some general principles in this field should be mentioned.

The role of liver resection as an effective treatment for LMCC was solidified by the report from the registry of hepatic metastases in 1988. They gleaned from a retrospective chart review of 859 patients who underwent liver resection for LMCC between 1948 and 1985. The 5-year actuarial survival rate and actuarial disease-free survival rate in all the patients were 33 and 21%, respectively.1

With the improvement of pre-operative and intraoperative imaging techniques, understanding of the vascular and surgical anatomy of the liver, application of new surgical instruments and technology, knowledge of tumour biology, pre-operative evaluation of liver function reserve, and identification of prognostic factors, operative mortality rate after major liver resection has been reduced to <3% in experienced hepatobiliary surgical centers, and the 5-year survival rate in LMCC after resection has reached 26–51%.1–5 The advancing of liver surgery has led to the reevaluation of the indication for resection of LMCC and applications of novel surgical approaches.

Nomenclature of hepatic anatomy and resections

The liver resection is founded on the anatomic system originally described in the early 1950s by Couinaud45 as well as Healey,46,47 who defined the intrahepatic divisions of blood vessels and bile ducts and established the subdivisions of the liver using corrosion casting. Their studies were a great advance for the science of hepatic anatomy, but caused a long-lasting confusion in terminology of both hepatic anatomy and hepatic resection in the following years of the 20th century. Descriptions of liver anatomy and of common liver resections have yielded a huge number of names which are very confusing and making it difficult for literature analyzing and communication among hepatic surgeons. Multiple terms are in use for the same anatomic structure or surgical operation, while one term might indicate different procedures. As a result, Strasberg presented a proposal for a uniform terminology in 1997,48 which led to the naissance of the first universally accepted terminology system ‘The Brisbane 2000 terminology of liver anatomy and resections’.49 This terminology is completely based on the internal anatomy, not the surface markers, in describing the several levels of division of the liver. It is rapidly gaining wide acceptance and has been adopted in the latest 39th edition of Gray’s Anatomy. The terminology system is illustrated in Table 1, which shows the successive orders of division and the terminology for resections involving three sections.

Table 1
Brisbane 2000 terminology of liver anatomy and resections49

<table>
<thead>
<tr>
<th>Division order</th>
<th>Anatomical term</th>
<th>Couinaud segments referred to</th>
<th>Term for surgical resection</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-order division</td>
<td>Right hemiliver OR right liver</td>
<td>Sg 5–8 (± Sg 1)</td>
<td>Right hepatectomy OR right hemihepatectomy (stipulate ± Sg 1)</td>
</tr>
<tr>
<td></td>
<td>Left hemiliver OR left liver</td>
<td>Sg 2–4 (± Sg 1)</td>
<td>Left hepatectomy OR left hemihepatectomy (stipulate ± Sg 1)</td>
</tr>
<tr>
<td>Second-order division</td>
<td>Right anterior section OR right paramedian section</td>
<td>Sg 5.8</td>
<td>Add (-ectomy) to any of the anatomical terms</td>
</tr>
<tr>
<td></td>
<td>Right posterior section OR right later section</td>
<td>Sg 6.7</td>
<td>Right posterior sectionectomy OR right lateral sectionectomy</td>
</tr>
<tr>
<td></td>
<td>Left medial section</td>
<td>Sg 4</td>
<td>Left median sectionectomy OR resection segment 4 OR segmentectomy 4</td>
</tr>
<tr>
<td>Third-order division</td>
<td>Segments 1–9</td>
<td>Sg 2.3</td>
<td>Left lateral sectionectomy OR bisectionectomy 2,3</td>
</tr>
<tr>
<td></td>
<td>Any one of Sg 1–9</td>
<td>Any one of Sg 1–9</td>
<td>Segmentectomy</td>
</tr>
<tr>
<td></td>
<td>Two continuous segments in continuity</td>
<td>Any two of Sg 1–Sg 9</td>
<td>Bisectionectomy</td>
</tr>
<tr>
<td>Resections of three sections</td>
<td>Sg 4–8 (± Sg 1)</td>
<td>Sg 2,3,4,5,8 (± Sg 1)</td>
<td>Right trisectionectomy OR extended right hepatectomy OR extended right hemihepatectomy (stipulate ± Sg 1)</td>
</tr>
</tbody>
</table>

a The right/left trisegmentectomy are preferred terms.
Reevaluation before surgical procedure

As with all the other abdominal cancer surgeries, the first operative step is to exclude the presence of any contraindications to hepatic resection, such as the existence of unresectable hepatic or extrahepatic disease. Sampling of suspected lesions is of great importance.

The use of intraoperative ultrasound is stressed by many authors and has been considered to be the most sensitive method in thoroughly assessing the extent of hepatic metastases. It can provide information regarding the number of metastases, as well as proximity to major vascular structures. Using this method, approximately 15–25% of patients, new metastases not identified by pre-operative imaging could be identified.\(^50,51\) Understandably the use of intraoperative ultrasound could change the operative management in about 15% of patients.\(^51,52\)

Colorectal cancer with synchronous liver metastases

Synchronous liver metastases represent about 20–30% of newly diagnosed colorectal cancers,\(^1\) among whom resectable hepatic lesions are seen in 10–25% of the stage IV patients.\(^53–55\) However, consensus has not been reached as to the timing of surgical resection of hepatic metastases and the colorectal primary in this large group of patients. Some researchers consider that the survival benefit from hepatic resection is determined by the biologic behavior of the neoplasm rather than by early detection, while some others reported higher complication and mortality rates for those with simultaneous resection of the colon and liver. Nordlinger et al. reported an operative mortality of 7% for simultaneous resections, compared with 2% (\(P < 0.01\)) for staged resections.\(^5\) In the series of Bolton and Fuhrman, the reported operative mortality is 12% for simultaneous surgeries. For those involving major liver resections, the operative mortality is as high as 24%.\(^56\) As a result, a ‘test of time’ or delayed hepatic resection has been recommended, either to fully evaluate the biologic features of the disease\(^57–60\) or to improve the perioperative outcomes.\(^56–62\)

In recent years, along with the increasing number of studies reporting good results for simultaneous procedures, the paradigm for the surgical management of synchronous colorectal metastases has begun to change. In their reports, the survival rates, post-operative mortality and perioperative morbidity are comparable, whether the procedures were carried out simultaneously or in a staged manner.\(^63–65\) It is noteworthy to mention the fact that very few reports in the new millennium are still strongly opposing the simultaneous procedure.

Though it seems that a consensus has almost reached, we have to be aware that all the studies available were of retrospective nature, the reported data were from institutions and surgeons with definitely different experience of liver resection, and the selection factors that led the surgeons to perform simultaneous or staged procedures were widely different. A well-designed, prospective, randomized, multicenter study is highly demanded before its use could be advocated.

In current practice, a simultaneous resection is more often associated with right colonic primaries and when only a single metastatic lesion was found in the liver, while a staged resection is more often associated with rectal primaries or multiple liver lesions. But further analysis of patients in different subgroups according to the location of primary tumours and extent of hepatic resection did not reveal a particular group who are in unacceptably high risk when performing simultaneous colon and liver resection. This indicates that the operating surgeons appeared to be the most important determinant in patient selection. Before the controversy is really solved, no definite indications or contraindications to simultaneous resection could be established. The final decision should be made by the operating surgeons based on the experience and comfort level of the team. Now that more and more studies have revealed that simultaneous resection of the primary colorectal tumour and hepatic metastasis is highly efficient without sacrificing the safety, saving the patient from a second laparotomy, and is better for patients both psychologically and economically, it should be considered the preferred treatment for selected patients with resectable synchronous colorectal metastases.

Repeated resections for recurrent metastases

Despite the careful selection of patients and the curative intent of surgery, 60–70% of patients undergoing liver resection for LMCC will develop recurrent disease. The liver is the most common site of recurrence and might be the only site in about one third of those who recur.\(^20,66\) In recent years, repeated hepatectomy for recurrences is increasing due to the advances in the early detection, novel chemotherapeutic agents, and the expertise of liver resection. To these patients, it has been demonstrated that second, even third hepatectomies have similar morbidity, mortality and impacts on survival, compared with the first liver resections.\(^67–70\) Not surprisingly, the same prognostic factors that predict favorable outcome after the primary resection apply to the repeated liver resection, including complete removal of metastatic lesions with satisfactory margins, no extrahepatic disease, etc.\(^68,69\)

Methods of improving resectability

For LMCC, the prime goal of liver resection is complete tumour removal with at least macroscopically clear margins and with minimal operative risk. Due to the advances of liver surgery, there is at present almost no location in the liver where tumours could not be resected technically. But still approximately 80–90% of patients with liver metastases of colorectal cancer are not candidates for curative resections at diagnosis. Apart from the fitness of patients,
the unresectability of liver lesions could usually be ascribed to the following two major reasons. First, technically unable to remove the tumour(s) completely due to the number, size, location and distribution of the metastases. This is the main cause of unresectability. Second, biologically there exist some negative prognostic factors that preclude the patients from gaining potential benefits from surgical resection. But as we have pointed out previously, the spectrum of prognostic factors is changing as our knowledge accumulates. What might be a potent prognostic factor and contraindication today could be demonstrated to contribute little to the survival in the future. Actually this already happened for some factors, such as the number, size and distribution of metastases, and the extent of the resection margin, none of them seem to be as important as previously considered. A R0 resection could be achieved both intrahepatically and extrahepatically.4,23,31,71 The approaches described below are used alone or in tailored combinations, targeting to improve the resectabilities.

Chemotherapy

With the dramatically improved response rate associated with the advances in chemotherapy for colorectal cancer, neoadjuvant approach is gaining wider use as a potential modality to render primarily unresectable patients resectable. Even in originally resectable patients, neoadjuvant chemotherapy might also increase the R0 resection rate and facilitate limited hepatectomies. The rationale for neoadjuvant chemotherapy also lies in that the response could be used as a stratification criterion to exclude the patients with particularly aggressive disease from inappropriate surgery.24 Additionally, pre-operative chemotherapy could be considered as a chemosensitivity test in vivo, which would help to modulate the strategy of the future chemotherapy. As long as the efficacy is concerned, satisfactory hepatic resection after tumour response to chemotherapy could provide a possibility of long-term survival comparable to that of the primarily resected patients.72

5-Fluorouracil (5-FU) has been used as the treatment of choice for almost five decades,73 but the result was far from satisfaction until the emergence of the novel agents of oxaliplatin and irinotecan. Modern chemotherapeutic protocols combining 5-FU, leucovorin (LV) and oxaliplatin or 5-FU, leucovorin and irinotecan or the combining use of oxaliplatin and irinotecan have demonstrated superior response rates around 50% in phase III clinical trials,74-77 compared with almost all the protocols ever used. Though the optimal neoadjuvant systemic chemotherapy regimen has yet to be determined, most reports suggested that infusional FU/LV with oxaliplatin and/or irinotecan are the most effective protocols for this purpose.74-77 However, although the response rates are very high when used as the first-line therapy, the response rates for second-line therapy are as disappointingly low as 10–20%, even when the most potent protocols are used.78-80 So patients with tumour progressing while on chemotherapy usually have a low likelihood of being rendered resectable with second-line systemic chemotherapy.

Besides systemic use, neoadjuvant chemotherapy via the hepatic arterial infusion (HAI) has also been used and demonstrated high response rate in both the first- and second-line settings.51-83 The major advantage of HAI over systemic chemotherapy is the possibility to achieve higher drug concentrations at the tumour while reducing systemic exposure and hence side-effects. Generally, the ideal candidates for HAI chemotherapy are patients with metastatic lesions confined to the liver, with good performance status, no severe ascites or hyperbilirubinemia.84-86 Recently, preliminary data from several clinical trials using the oxaliplatin or irinotecan via HAI have demonstrated a promising future.87-89

What’s new and worth mentioning in this field is that significant progress in molecular biology has produced a great number of new ‘biologically targeted’ drugs that are now in various stages of clinical development. Two of these drugs, bevacizumab and cetuximab, which are monoclonal antibodies against vascular endothelial growth factor A (VEGF-A) and epidermal growth factor receptor (EGFR), respectively, have already significantly impacted the survival of patients with advanced colorectal cancer when integrated with chemotherapy in clinical trials.90-93 They both were approved for use in metastatic colorectal cancer by FDA and European Commission in 2004 and early 2005.

Portal vein embolization and two-stage hepatectomy

Despite great advances in hepatic surgery, insufficient functional remnant liver parenchyma after complete tumour removal remains one of the major reasons for unresectabilities. Generally, if no more than 30% of the total liver parenchyma could be remained after resection, the risk of post-operative liver failure would be very high, which contributes most to post-operative mortality. Some authors even advocated that 40% should be taken as a safe threshold in patients accepted prolonged chemotherapy.94 Portal vein embolization (PVE), which was first described by Makuuchi et al. in the early 1980s,95 can induce homolateral atrophy of the liver to be resected and contralateral compensatory hypertrophy of the remnant liver, thus increasing both the resectability of patients with liver tumours and the safety of the surgery.96-98 So PVE is indicated for those that resection of a large portion of the functional liver parenchyma is technically feasible, but the surgery is contradicted by a too small size of remnant liver. In one series, 63% of originally unresectable LMCC could be converted to resectable by pre-operative PVE. What’s more impressive was that the 5-year survival rate could be as high as 40%, comparable to that of initially resectable patients.99 One of a recent retrospective studies further demonstrated that the pre-operative PVE might reduce the intrahepatic recurrence after liver resection for unilobar LMCC.100
Despite the advantages of PVE in hepatic surgery, its negative aspects have also appeared as more experience collected. Apart from the technical complications caused by the procedure itself, including thrombosis and/or migration of the emboli in the contralateral hepatic lobe, hemoperitoneum, hemobilia and transient liver insufficiency, which will occur in approximately 10% of the patients undergoing the procedure percutaneously and usually easy to treat, the most concerned is that PVE stimulates the growth of tumours in the contralateral liver, although the exact mechanism is unknown. In order to take full advantages of the PVE while surmount the possible disadvantage of tumour-growth stimulation, Jaeck and colleagues adopted a rational modality from 1996, which was called ‘two-stage hepatectomy procedure (TSHP)’ combined with PVE’ in selected patients with initially unresectable multiple and bilobar liver lesions. In the first-stage laparotomy, one hemiliver is completely cleared of metastatic lesions by hepatic resection and/or radiofrequency. A subsequent PVE to the contralateral hemiliver will then be followed to induce atrophy and hypertrophy in the to-be-resected and future remnant hemilivers, respectively. Finally a second-stage hepatectomy will be carried out to completely remove the metastases-involved liver. Their experience demonstrated that this strategy could be carried out safely and effectively in selected patients with initially unresectable multiple bilobar colorectal liver metastases. The 5-year survival is comparable to those with initially resectable liver metastases.

Locally ablative modalities

As for any surgical procedure there are patients, and situations, in which the risk of major liver resection is too high compared with the potential benefits. Under this circumstances, locally ablative modalities, such as radiofrequency ablation (RFA), cryotherapy or high intensity focused ultrasound (HIFU) could be alternative options, either used independently or as an adjunct to surgery. RFA has been more widely utilized. It could be used percutaneously, via laparoscopy or through a laparotomy. The most dominant limitations of most ablative modalities are the tumour size limit and not applicable to those adjacent to major biliary or vascular vessels and important viscera.

The place of laparoscopic surgery in LMCC

The evolution of laparoscopic surgery has made it a must-to-mention in almost all the topics concerning abdominal surgery. Its role in pre-operative assessment for LMCC has been mentioned previously, but its application in liver resection is gaining more enthusiasm recently and is currently at the forefront of the minimally invasive surgery. Unlike other abdominal surgeries, the laparoscopic approach for liver resections has been slow to gain wide application, due to the technical difficulties and considerations of oncologic adequacy. Since, the first report of anatomic liver resection in 1996, an increasing number of publications have emerged in reference to the laparoscopic treatment of liver tumours. Unfortunately, so far almost all literatures published in this field are still limited to feasibility and safety studies, and the majority of the reports have emanated from some European centers. Even for these reports, they have mostly concentrated on replicating traditional open hepatic resection techniques via a laparoscopic approach. At present, several issues could be stated based on the literature review: (1) laparoscopic liver resection is an advanced procedure that should be performed by surgeons with a combination of expertise in both laparoscopic and hepatobiliary surgery. Major hepatic resection should not be performed until significant experience is obtained; (2) control of bleeding is always a great challenge; (3) the oncologic integrity of the procedure remains unproven.

Recently Vibert and colleagues reported that after laparoscopic hepatic resection, the 3-year overall and disease-free survival rates for the 37 patients with LMCC could be as high as 87% and 51%, respectively. A previous multicenter study reported a 2-year survival of 53% in 10 patients of LMCC. Apart from the pre-selection of patients for the procedure, laparoscopic hepatic resection seemed to be a promising approach for selected LMCC patients. If the survival data could be confirmed in future prospective, randomized and well-controlled trials, it might facilitate a multimodal treatment for patients with LMCC, including repeat resections and/or ablation of non-resectable lesions.

Conclusions

The concept of LMCC has dramatically changed in the past 20 years. A consensus has been established that hepatic resection is the only treatment that could provide the patients the greatest probability of long-term survival. The present principle as to the resectability is that resection should be performed if all the metastases could be removed while leaving sufficient functional hepatic parenchyma, regardless of their size, number, location or distribution. Even if there exist EHDs, curative effect could still be possible if a complete surgical resection could be carried out.

For better mutual understanding and communication, we advocate using the Brisbane 2000 terminology system as a uniform nomenclature in describing hepatic anatomy and resection.

Proper use of modern chemotherapy, PVE and/or two-stage hepatectomy, and the local ablative modalities might improve the respectability and survival. Pre-operative FNA biopsy should be avoided in potentially curative patients.

Laparoscopic approach might be a promising option for LMCC, but should be strictly limited to experienced hands and its oncologic adequacy still remains unestablished.
To optimize the treatment for LMCC, it is of utmost importance that a multidisciplinary team, consisting of oncologists, radiologists, and surgeons should collaborate closely.

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