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Laparoscopic hepatectomy significantly shortens the time to postoperative chemotherapy in patients undergoing major hepatectomies

Nsehniitooh Mbah, MD, Steven C. Agle, MD, MPH, Prejesh Philips, MD, Michael E. Egger, MD, MPH, Charles R. Scoggins, MD, MBA, Kelly M. McMasters, MD, PhD, Robert C.G. Martin, MD, PhD *

University of Louisville, Department of Surgery, Division of Surgical Oncology, Louisville, KY, USA

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ABSTRACT

Background: The benefit of adjuvant chemotherapy occurs with early initiation, but is commonly delayed due to postoperative complications. Minimally invasive surgery is proven to significantly reduce complications and hospital length of stay. This study compares open versus laparoscopic liver resection in patients requiring adjuvant chemotherapy.

Methods: 120 consecutive patients with metastatic colorectal liver cancer who underwent liver resection between 2007 through 2012 were reviewed from an IRB prospective database.

Results: 44 laparoscopic cases were compared to 76 open cases having equivalent resections. Laparoscopic liver resection patients had lower blood loss (276 ml) than patients with open resection (614 ml). Patients with laparoscopy had shorter length of hospital stay (5 days) than patients with open resection (9 days). Patients with laparoscopic resection had a shorter time of chemotherapy initiation postoperatively (24 days v 39 days). Overall complication rates were higher, but statistically insignificant in patients with open resection.

Conclusions: Our data showed that the shorter LOS with laparoscopic major hepatectomies allows earlier initiation of chemotherapy compared to the open group, without jeopardizing surgical margins or extent of resection.

Summary: Over the past decade multiple authors have established that, despite occasional longer operating times, laparoscopic liver surgery is associated with reduced blood loss, reduced postoperative morbidity and shorter hospital stay. The purpose of this analysis was to determine if the advantages of a minimally invasive approach correspond to shorter initiation of adjuvant chemotherapy versus an open approach.

1. Introduction

The majority of hepatic cancer in the United States is metastatic colorectal cancer. Advanced technology and surgeons' experience have provided different treatment options for resectable metastatic colorectal cancer. These include laparoscopic and open hepatectomies, plus/minus chemotherapy.[1] Despite these options, a major hepatic resection is an extensive operation with consequent risks of morbidity and mortality. As compared with open hepatic lobectomy, laparoscopic hepatic lobectomy carries a substantial learning curve, as well as the potential for improved perioperative outcomes. The use of laparoscopic surgery to manage hepatic metastases was reported as early as 1993,[2] and in 2008 experts in hepatobiliary surgery participated in a conference held in Louisville KY, USA and demonstrated and came to consensus on the safety and effectiveness of laparoscopic liver resection.[3] Despite its comparability with open liver resection, concerns remain about the risks of major hemorrhage, gas embolism, and dissemination of malignant tumors.[4,5] These concerns have been responsible for the initial slow adoption of this operation through the laparoscopic approach in benign and malignant diseases.[6–8] At this point, multiple authors have established that, despite occasional longer operating times, laparoscopic liver surgery is associated with reduced blood loss,

* Corresponding author. Division of Surgical Oncology, University of Louisville, 315 East Broadway, #313, Louisville, KY 40202, USA.
E-mail address: Robert.Martin@louisville.edu (R.C.G. Martin).

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reduced postoperative morbidity and shorter hospital stay.[9–12] This has culminated in the recent consensus of the laparoscopic approach as an appropriate option for certain hepatic procedures including hepatic lobectomy and other major hepatic resections.[13–15] The purpose of this analysis was to determine if the advantages of a minimally invasive approach correspond to shorter initiation of adjuvant chemotherapy versus an open approach.

2. Methods

This was a review of our prospective database of patients who underwent hepatectomies for colorectal cancer with liver metastases from 2007 to 2012 at the University of Louisville Hospital in Louisville, KY. The study protocol was approved by the Institutional Review Broad (IRB), and all patients provided written, informed consent. Upon enrollment, a study coordinator, research assistant, or investigator obtained the patient's medical history and demographic information. All patients underwent hepatectomies carried out by a previously described protocol.[16,17]

In total, 120 patients were identified and stratified into two groups, laparoscopy verses open resection. In the laparoscopic hepatectomy cohort, both pure laparoscopic and hand-assisted techniques were grouped together. The decision to perform a laparoscopic major hepatectomy was determined by the treating hepatobiliary surgeon based on the size of tumor, location of tumor, histology of tumor, and the ability to achieve an acceptable oncologic margin. Only patients undergoing a major hepatectomy were included in this evaluation; patients undergoing hepatic ablation or other extrahepatic procedures were included as long as a major resection was also undertaken. In patients undergoing hepatic resections, anatomic segmental liver resections were performed and classified as described by Couinaud.[18,19] A major hepatectomy was defined as removal of three or more Couinaud segments. All of these types of major hepatectomies were included in the analysis except for extended left lobectomy because of the significantly disproportionate number of open cases compared to laparoscopic approaches.

In the time from 2007 to 2012, our group used the 2006 Society of Surgical Oncology and the American Hepato-Pancreatico-Biliary Association Consensus Conference definition of resectability, defined as the ability to resect all visible disease and leave enough liver behind for an appropriate recovery time.[20] Demographics recorded for each group included age, gender, race, types of cancer and indication for surgery. (Table 1). Similarly, our group universally agrees that a high-risk metastatic colorectal score $\geq$3 should undergo some form of adjuvant chemotherapy.[21]

The technique for anesthetic management during hepatectomy has been reported previously.[22] In principle, we use a low central venous pressure (<5 mmHg) and maintain a urine output of >25 mL/h and a systolic blood pressure of >90 mmHg during parenchymal transection. After the specimen is removed, crystalloid is administered intravenously to achieve euvolemia. Packed red blood cells and autologous blood was usually given to maintain hemoglobin of >10 g/dL in patients with evidence of either coronary or cerebrovascular disease. Intraoperative blood products are not administered until blood loss exceeds 25% of the total blood volume.

The technique for laparoscopic right and left hepatectomy in a majority of cases places the patient supine, in steep reverse Trendelenburg, with slight rotation to either left or right, based on the side to be resected. After trocar placement and mobilization of the liver, a complete hepatic ultrasound of the liver is performed to define anatomy, location of tumor(s), and to ensure remnant liver is free of disease or abnormalities that would change surgical management. After adequate mobilization, the line of liver resection is demarcated with electrocauterization, with initial liver transection performed with a hemostatic assist device. Deep parenchymal transection including inflow and outflow control was obtained using a vascular stapler. In a majority of the laparoscopic patients, inflow and outflow is controlled intraparenchymally, and extrahepatic inflow and outflow dissection and control were not performed. On the rare occasions intermittent inflow vascular occlusion (the Pringle maneuver) was used, it was applied in 5- to 10-min intervals, released briefly, and reapplied as necessary.[23] Open hepatectomy was performed using standard techniques, as described previously, commonly using the crush-and-clip technique or with a hemostatic assist device for parenchymal transection.[24] This initial dissection was followed by inflow and outflow control that was obtained using a vascular stapler.

All postoperative complications were recorded and graded by using a standard classification scale of complications (Clavien), which has been reported previously.[16,17] Postoperative complications evaluated included estimated blood loss, transfusion requirement, any complication (e.g., cellulitis, urinary retention, ileus, shortness of breath), wound infection, 30-day readmission and 90-day mortality.

Table 1
Published studies on chemotherapy for resectable colorectal cancer with liver metastases.

Author, Pub. Year	Patients	Study Type	Study Period	Study Group	Conclusions
Tohme et al.[25]	508	Retrospective Cohort Study	2009–2013	Determine differences in timing to post-operative chemotherapy between laparoscopic and open liver resection for metastatic colorectal cancer	Modifying deleterious effects of postoperative complications, patients undergoing laparoscopic surgery are treated soon compared to open.
Day et al.[31]	209	Retrospective Analysis	2003–2010	Determine if Patients who receive adjuvant chemotherapy in <8 weeks following surgery can have improved survival	There is overall survival when patients receive adjuvant chemotherapy in less than 8 weeks
Biagi et al.[29]	15410	Meta-analysis	1975–2011	Determine the relationship between time to adjuvant chemotherapy and survival outcomes via systemic and meta-analysis	Longer time to adjuvant chemotherapy was associated with worse survival among patient with resectal colorectal cancer
Nordlinger et al.[27]	364	Randomized controlled trial	2000–2004	Assessing the combination of perioperative chemotherapy and surgery compared with surgery alone in patients with initially resectable liver metastases from colorectal cancer	Perioperative chemotherapy with FOLFOX4 is compatible with major surgery and reduces risk of events of progression-free survival in eligible and resected patients
Mitry et al.[28]	278	Two randomized Trials	62.2 months	Systemic chemotherapy after surgical resection of colorectal cancer with metastases may reduce the risk for recurrence and improve survival, but its benefits has never been demonstrated.	There is a marginal statistical significance in fovar of adjuvant chemotherapy with an FU bolus-based regimen after complete resection of colorectal cancer metastases.