ORIGINAL ARTICLE

Long-term survival in laparoscopic vs open resection for colorectal liver metastases: inverse probability of treatment weighting using propensity scores

Joel W. Lewin[1], Nicholas A. O'Rourke[1,2], Adrian K.H. Chiow[1], Richard Bryant[1,3], Ian Martin[2], Leslie K. Nathanson[2,3] & David J. Cavallucci[1,2]

[1]Hepato-Pancreato-Biliary Surgery, Royal Brisbane & Women's Hospital, [2]General Surgery, The Wesley Hospital, and [3]General Surgery, Holy Spirit Northside Hospital, Australia

Abstract

Background: This study compares long-term outcomes between intention-to-treat laparoscopic and open approaches to colorectal liver metastases (CLM), using inverse probability of treatment weighting (IPTW) based on propensity scores to control for selection bias.

Method: Patients undergoing liver resection for CLM by 5 surgeons at 3 institutions from 2000 to early 2014 were analysed. IPTW based on propensity scores were generated and used to assess the marginal treatment effect of the laparoscopic approach via a weighted Cox proportional hazards model.

Results: A total of 298 operations were performed in 256 patients. 7 patients with planned two-stage resections were excluded leaving 284 operations in 249 patients for analysis. After IPTW, the population was well balanced. With a median follow up of 36 months, 5-year overall survival (OS) and recurrence-free survival (RFS) for the cohort were 59% and 38%. 146 laparoscopic procedures were performed in 140 patients, with weighted 5-year OS and RFS of 54% and 36% respectively. In the open group, 138 procedures were performed in 122 patients, with a weighted 5-year OS and RFS of 63% and 38% respectively. There was no significant difference between the two groups in terms of OS or RFS.

Conclusion: In the Brisbane experience, after accounting for bias in treatment assignment, long term survival after LLR for CLM is equivalent to outcomes in open surgery.

Received 12 August 2015; accepted 21 August 2015

Correspondence

Joel W. Lewin, Royal Brisbane Hospital, Butterfield Street, Herston, QLD, 4006, Australia. E-mail: joel.lewin@uqconnect.edu.au

Introduction

The liver is the most common non-nodal site affected by colorectal cancer metastases, with approximately 60% of all patients having developed liver metastases by 5 years following diagnosis.[1] The role of hepatectomy for colorectal liver metastases (CLM) is well established, with open resection series reporting 5-year overall survival (OS) between 37 and 45%.

The application of laparoscopy to liver resection for malignancy remains somewhat controversial in the absence of randomised controlled trials to confirm oncologic equivalence to the open approach. With increasing experience and wider application of laparoscopic liver resection (LLR), much enthusiasm has been directed towards its use in CLM. Since the initial reports of LLR in the early nineties,[2–5] there has been a steady increase in its use for both benign and malignant conditions. A recent study on the international experience with laparoscopic liver resection at 11 experienced centers reported 5388 LLRs and 1184 major LLRs, over half of which were for malignancy.[6]

The short term benefits of a laparoscopic approach to liver resection compared to open are well described,[7,8] including reduced postoperative pain and analgesia requirement, smaller incisions, less wound complications, reduced hospital length of stay (LOS)[9,10] and even reduced overall cost.[11,12] There is, however, a relative paucity of quality studies comparing survival and long-term outcomes for open versus laparoscopic resection of CLM.

This study was presented at the 2014 Biennial IHPBA conference in Seoul, South Korea as an oral presentation.

Our unit began LLR for CLM in 1999, with the first laparoscopic right hepatectomy performed in 2000. A randomised controlled trial (RCT) comparing laparoscopic to open hepatectomy for malignancy remains difficult to achieve, therefore this study attempts to maximise the utility of collected observational data by using statistical tools that enable balance across treatment and control groups.

Propensity score-based analyses have grown in popularity in recent years, in large part due to the promise of reducing confounding inherent in observational cohort studies. Inverse probability of treatment weighting (IPTW) using the propensity score has a number of potential advantages over more common matching techniques. Evaluating data using these models adds some statistical complexity, however if well specified, can allow estimation of causal effects from observational data.

Method

Patient selection

Ethics approval was obtained for a retrospective review of prospectively collected data, involving patients undergoing liver resection for CLM from 2000 to 2014. Five surgeons (NO'R, LN, IM, RB, DC) at three Brisbane institutions (RBWH, TWH, HSNH) during that period performed all operations. Patient demographics, operative details and data on both intraoperative and postoperative adverse events were recorded prospectively from 2004 in a secure hepatic surgery database. Data from before this period was obtained retrospectively. Details of the colorectal primary (size, location, lymph node status, differentiation and operative details), burden of liver disease (tumour number, location, diameter, total tumour volume) and CEA were collected. Clinical Risk Scores[13] and pre- and postoperative Basingstoke Predictive Index (BPI) scores[14] were determined from their component factors at the time of data analysis.

Preoperative patient management

Diagnosis of liver metastases was made with either high definition, multiphase, computed tomography (CT) or more recently, magnetic resonance imaging (MRI) with liver specific contrast (Gd-EOB-DTPA, Primovist™ or Eovist™).[15–17] Positron emission tomography (PET) imaging was used routinely since becoming available in 2004, to exclude extrahepatic disease.

Patients were discussed at a multidisciplinary team meeting (MDT). Pseudo-neoadjuvant and/or adjuvant chemotherapy was used as per consensus after discussion at MDT. Whether a patient was to receive open or laparoscopic resection had no influence on the overall chemotherapy approach determined at MDT. All surgeons had experience in, and offered both laparoscopic and open surgery. If the projected remnant liver was less than 30% of total liver volume, if the risk of postoperative liver insufficiency was high, or if patients had resectable bilobar disease, portal vein embolisation or ligation, and/or 2-step staged hepatectomy was used.[18]

Operative techniques

Over the study period, techniques of both laparoscopic and open liver surgery have evolved. Open liver resection was performed using standard techniques. For major hepatectomy, extrahepatic division of the portal vein, hepatic artery and hepatic veins with parenchymal transection using CUSA™ (Cavitron Ultrasonic Surgical Aspirator, Tyco Healthcare, Mansfield, MA, USA) was most commonly used.

Most laparoscopic resections were performed in a "pure" fashion, with specimen extraction following the end of the hepatectomy via a Pfannenstiel incision or extension of the umbilical port site. Occasionally, "hybrid" and "hand-assisted" techniques were performed. Laparoscopic ultrasound was performed to confirm the number and location of lesions. Parenchymal division has evolved from the use of stapling devices and Harmonic Shears® (Ethicon Endo-Surgery, Cincinnati, OH, USA) to "hot" Kelly-clysis using a laparoscopic dolphin tip Ligasure™ (Covidien, Mansfield, MA) with copious irrigation. Hem-o-lok® clips (Weck Surgical Instruments, Teleflex Medical, Durham, NC) were used for vascular control with occasional stapler use for larger vessels.[19]

The Brisbane terminology[20] was used for classifying all liver resections. Intraoperative complications were classified as grade I, II or III, based on the Satava classification of intraoperative incidents[21] adapted for LLR.[22]

Postoperative management

Patients were occasionally admitted to ICU postoperatively, based on the presence of significant preoperative comorbidities or intraoperative surgical or anaesthetic complications. Standard postoperative cares included chemical and mechanical DVT prophylaxis, postoperative analgesia, monitoring of liver function and early mobilisation. Postoperative analgesia was most often intravenous patient-controlled analgesia and non-steroidal anti-inflammatories. Epidural and single-shot intrathecal analgesia were used occasionally.

Postoperative complications were graded and recorded using the Dindo-Clavien classification.[23] Routine postoperative follow-up consisted of clinical assessment and CEA levels at 3, 6, 12, 18 and 24 months, then annually, with imaging performed at 6 monthly intervals or sooner, if indicated. Recurrent disease was diagnosed on imaging and included disease at extrahepatic sites. RFS was defined as time from resection until the development of a recurrence, either hepatic or extrahepatic, or death. OS was measured from study entry until death (any cause).

Statistics and survival analysis

Data was considered on an intention-to-treat (ITT) basis, such that patients who required conversion to hand assist, hybrid or open approach, were included in the laparoscopic group. Propensity scores were generated using generalised boosted modelling (GBM) logistic regression modelling. Based on available evidence,[7] preoperative baseline covariates were selected to