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Outcomes after repeat hepatic resection for recurrent metastatic colorectal cancer: A population-based study

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Abstract

BACKGROUND: More than half of the patients undergoing resection for colorectal cancer liver metastases develop recurrent hepatic disease. We report management and outcomes of patients undergoing repeat hepatectomy in routine practice.

METHODS: All cases of repeat hepatectomy for colorectal cancer liver metastases from 2002 to 2009 in the Canadian Province of Ontario were identified using the population-based Ontario Cancer Registry and linked treatment records.

RESULTS: Of 1,310 patients who underwent resection of CRLM, 78 (6.0%) underwent a repeat liver resection. Mean age was 56 years and the median time between resections was 19 months. Compared with the first resection, second resections were associated with fewer lesions (2.7 vs 1.5; $P = .001$) and fewer major resections (58% vs 31%; $P = .024$). The size of largest lesion, positive margin rate, length of hospital stay, and 90-day mortality were similar. Unadjusted 5-year overall survival from the time of second resection was 45% (95% confidence interval = 32% to 59%) and cancer-specific survival was 47% (95% confidence interval = 30% to 64%).

CONCLUSIONS: Repeat liver resections for metastatic CRC involve fewer lesions and less extensive surgery and a substantial proportion of patients achieve long-term survival.

Colorectal cancer is the second-leading cause of cancer death in the United States.[1] Liver metastases are diagnosed synchronously in up to 15% of patients, and another 15% will develop metachronous hepatic disease.[2–4] Hepatectomy is considered standard management for patients with resectable colorectal cancer liver metastases (CRCLMs) and is associated with 5-year overall survival (OS) rates of 39% to 58%.[5–11] However, recurrent disease occurs in 60% to 84% of the patients, with 60% recurring in the liver.[9,12,13]

While early reports of postoperative mortality for liver resection were close to 30%, in the modern era it is closer to 1%.[14,15] In addition, new concepts and techniques in hepatectomy such as parenchyma-sparing[16,17] and portal vein embolization[18,19] have expanded the patient population able to undergo complete extirpation of CRCLM. Ablative therapies have increased this population even

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further.[11,20–25] These advances have allowed for more aggressive surgical approaches such as 2-stage hepatectomies, simultaneous colon and liver resections, multivisceral resections, and repeat resections.

Repeat hepatectomies for recurrent CRCLM can be associated with long-term survival. As early as 1989, series regarding repeat hepatectomy for CRLM have been described.[26] Most published reports describe single-institution series, and it is unclear whether similar outcomes are being realized in routine clinical practice. To our knowledge, there are no published studies that describe utilization and outcome of repeat hepatectomy for metastatic CRC in a population-based approach. Population-based studies provide insight into management and outcomes achieved in routine practice and are less limited by referral and selection biases that plague traditional institutional case series. Moreover, they provide insight into the extent of adoption and access to novel therapies in routine care.[27,28] The objective of this study was to describe management and outcomes in a population-based cohort of patients undergoing repeat hepatectomy for CRCLMs.

Methods

Study design and population

This is a population-based, retrospective cohort study to describe the management and the outcome of resected CRCLM in the Canadian province of Ontario. Ontario has a population of approximately 13.5 million people and a single-payer universal health insurance program. The study population included all patients with CRC who underwent liver resection during 2002 to 2009. To identify the study cohort, we used the Ontario Cancer Registry to identify all incident cases of CRC in Ontario diagnosed during 1996 to 2009. We then identified all cases of liver resection from 2002 to 2009. The Ontario Cancer Registry (OCR) does not capture diagnoses of second primary cancers. As such, cases with liver resection more than 72 months after initial CRC diagnosis were excluded since those cases would likely represent recurrence of a second primary cancer. Cases with histology other than adenocarcinoma were excluded. To minimize mis-classification of liver metastases we also excluded cases with a second primary liver, biliary or pancreas cancer. Extent of liver metastases was not available in the existing data sources; for this reason we obtained surgical pathology reports for all potentially eligible cases. Patients with evidence of metastatic colorectal cancer as per the liver resection pathology report were included. Repeat hepatectomy was identified based on additional surgical pathology reports and/or linked hospital procedure administrative databases. Repeat resections performed within 6 months of the initial resection were considered planned 2-stage hepatectomies and were excluded from the study population. The study was approved by the Research Ethics Board of Queen's University.

Data sources and linkage

The OCR is a passive, population-based cancer registry that captures diagnostic and demographic information on at least 98% of all incident cases of cancer in the province of Ontario.[29] The OCR also provides information about vital status and cause of death. Records of hospitalization from the Canadian Institute for Health Information provided information about surgical interventions; these records are known to be complete.[30] Provincial physician billing records from the Ontario Health Insurance Plan, treatment records from regional cancer centers, and provincial records of chemotherapy delivery (New Drug Funding Program and Ontario Drug Benefits) were used to identify chemotherapy utilization. Incident cases of CRC identified from OCR were linked to other electronic administrative health databases at the Institute of Clinical and Evaluative Sciences. Surgical pathology reports were obtained from the OCR. A team of trained data abstractors reviewed the pathology reports and entered information about extent of disease and surgical procedure into an electronic database.

Measures and outcomes

Comorbidity was classified using the Charlson Index modified for administrative data based on all noncancer diagnoses recorded during any hospital admission within 5 years before surgery.[31] Preoperative chemotherapy was defined as chemotherapy given within 16 weeks before resection of CRCLM; postoperative chemotherapy was defined as treatment initiated within 16 weeks after surgery for CRCLM. OS and cancer-specific survival (CSS) were determined from resection of CRCLM. To account for possible cause of death miscoding, CSS included death from any cancer. Complete information about vital status in the OCR was available up to December 31, 2012; cause of death was available up to December 31, 2010.

Statistical analysis

Comparisons of proportions between study groups were made using the chi-square test. Comparisons of means and proportions between first and second resection were made using the paired Wilcoxon signed-rank test and McNemar test, respectively. OS and CSS were determined using the Kaplan-Meier method. Factors associated with OS and CSS were evaluated using the Cox proportional hazards regression model. Results were considered statistically significant at P-value less than .05. As per Institute of Clinical Evaluative Sciences policy cells with fewer than 6 cases were suppressed; results in these fields are reported as approximate values to ensure that the precise small cell value cannot be determined. All analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC).