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Liver resection is justified for patients with bilateral multiple colorectal liver metastases: A propensity-score-matched analysis

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Abstract

Background: Increasingly, patients with multiple colorectal liver metastases (CLM) are surgically treated. Some studies have shown that patients with bilobar and unilobar multiple CLM have similar outcomes, but other have shown that patients with bilobar CLM have worse outcomes after resection. We aimed to compare clinical outcomes of surgical treatment of bilobar and unilobar CLM using propensity score matching.

Methods: The single-institution study included patients who underwent hepatectomy for ≥3 histologically confirmed CLM during 1998–2014. Clinicopathologic characteristics and long-term outcomes were compared between patients with bilobar and unilobar CLM in a propensity-score-adjusted cohort.

Results: A total of 473 patients met the inclusion criteria, 271 (57%) with bilobar and 202 (43%) with unilobar CLM. In the propensity-score-matched population (bilobar, 170; unilobar, 170), no differences were observed according to the distribution of CLM except for a greater frequency of concomitant ablation, and R1 resection in the bilobar group. There was no difference between the bilobar and unilobar groups in 5-year overall survival rates (46% and 49%, respectively; P = 0.740) or 3-year recurrence-free survival rates (21% and 24%, respectively; P = 0.674).

Conclusions: Tumor distribution may not affect the curability of surgery for multiple CLM. Liver resection would be justified for selected patients with bilobar CLM.

Keywords: Colorectal liver metastases; Bilobar; Liver resection; Overall survival; Recurrence-free survival

Introduction

In the early 1990s, when resection of colorectal liver metastases (CLM) became a standard practice, patients with more than 3 lesions were excluded [1]. Now, however, thanks to advances in patient selection, systemic therapy, and liver resectional techniques [2], the presence of multiple lesions is no longer a contraindication to surgery for CLM [3]. Hepatic resection combined with perioperative chemotherapy has become the standard of care for patients with multiple CLM [4].

Resection of bilobar multiple CLM remains a challenge because it can be difficult to achieve margin-negative resection while preserving sufficient functional liver parenchyma to avoid postoperative hepatic insufficiency [5]. In the current era of multimodality treatment, some reports indicate

Abbreviations: CLM, colorectal liver metastases; RFA, radiofrequency ablation; RAS, rat sarcoma viral oncogene homolog; OS, overall survival; RFS, recurrence-free survival; CI, confidence intervals.

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that bilobar CLM are associated with a poor prognosis after resection [6–11]. However, with advanced surgical techniques and strategies (e.g., portal vein embolization, 2-stage hepatectomy and/or liver-first sequencing), an increasing number of patients with bilobar CLM have undergone curative surgical resection [5,12–14]. Some reports show that tumor distribution (bilobar or unilobar) does not influence the long-term outcome of patients with multiple CLM [15–20].

Primary lymph node metastasis, number of CLM, and diameter of largest metastasis have been reported to be prognostic factors in patients with CLM [21–23], and the number of CLM has been reported to be a particularly strong prognostic factor [24]. However, the impact of tumor distribution on prognosis has varied among studies [6–11,15–20], and no previous reports have had sufficient sample size to accurately evaluate the impact of tumor distribution on curability or prognosis. Hence, it is controversial whether bilobar distribution in itself is a poor prognostic factor or not.

Within this context, the primary aim of this study was to compare outcomes of surgically treated patients with bilobar CLM versus unilobar CLM using propensity score matching analysis.

Patients and methods

Study population and review of patient records

Approval of the Institutional Review Board of The University of Texas MD Anderson Cancer Center was obtained for this retrospective study (PA17-0394). From a prospectively maintained database, we identified 1971 consecutive patients who underwent liver resection for histologically confirmed CLM during the period from January 1998 through November 2014. Patients who underwent repeat hepatectomy for recurrence (n = 280), patients who did not undergo primary tumor resection or second-stage hepatectomy (n = 75), patients without at least 2 years of follow-up after hepatectomy (n = 205), and patients with fewer than 3 tumors (n = 938) were excluded, resulting in a final cohort of 473 patients (Fig. 1).

All patients were evaluated preoperatively with a baseline history and physical examination. Decisions about treatment were made collectively at a multidisciplinary liver tumor conference. Following preoperative chemotherapy, patients underwent re-staging, and surgical resection was offered to those patients whose tumors were considered resectable, defined as ability to achieve a negative margin while preserving more than 20%–30% of the total estimated liver volume, sparing 2 continuous hepatic segments, and maintaining vascular inflow and outflow and biliary drainage [25]. In patients with an anticipated insufficient standardized future liver remnant, preoperative portal vein embolization and staged hepatectomy were performed [14]. When it was not possible to design a resection that would permit complete tumor resection while leaving sufficient vascularized hepatic parenchyma to support postoperative hepatic function, radiofrequency ablation (RFA) combined with resection was performed [26,27].

The following data were recorded from the electronic medical record: sex, age, diagnosis, preoperative chemotherapy cycles and regimens, perioperative outcomes (estimated blood loss, blood transfusion, operative time, and surgical procedure), tumor characteristics (number of CLM and size of largest metastasis), and rat sarcoma viral oncogene homolog (*RAS*) mutation status. Postoperative complications were reviewed and classified according to the Clavien-Dindo classification. Complications classified as class IIIa or higher were defined as major [28]. Postoperative hepatic insufficiency was defined as a postoperative peak total bilirubin level in serum greater than 7 mg/dL [29]. Death from liver failure was calculated at 90 days after surgical resection or during the index admission.

Statistical analyses

Propensity scores were calculated as the single composite variable from a non-parsimonious multivariate logit-linked binary logistic regression of the baseline characteristics. Bilobar vs. unilobar CLM was the dependent variable [30,31]. The matching algorithm was based on logistic regression and included the following clinically relevant covariates: sex, age, body mass index, primary tumor site (colon or rectum), primary tumor lymph node status, time from primary diagnosis to CLM diagnosis, *RAS* status, number of CLM, and size of largest metastasis. Carcinoembryonic antigen level was not part of the propensity scores because of a large number of missing variables before preoperative chemotherapy. The matching procedure was performed as follows. First, caliper matching of the propensity score was applied with caliper size predefined as 0.2 of the standard deviation of the total sample. In a 1-pass procedure starting with a given patient with bilobar CLM, the closest match of a patient with unilobar CLM was identified. Next, covariates for bilobar vs. unilobar were compared. If covariates were equivalent or varied ≤10%, the pair of patients was retained for analysis and removed from the total sample to allow for the next matching cycle to take place. If covariates varied >10%, the pair was rejected. Then the first step of the matching process was repeated to identify the next closest match to the patient of the failed match according to the propensity score. Subsequently, a 1-to-1 match between the bilobar and unilobar groups was performed by the nearest-neighbor matching method within 0.2 standard deviations.

Continuous variables were compared using the Wilcoxon rank-sum test, and categorical variables were compared using the χ^2 test. Overall survival (OS) was measured from the date of hepatic resection to the date of death or last follow-up. Recurrence-free survival (RFS) was measured from the date of hepatic resection to the

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