Primary tumor location affects recurrence-free survival for patients with colorectal liver metastases after hepatectomy: A propensity score matched analysis

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Abstract
Background Whether primary tumor location of colorectal cancer (CRC) affects survival of patients after resection of liver metastases remains controversial. This study was conducted to investigate the differences in clinicopathological characteristics and prognosis between right-sided CRC and left-sided CRC patients with liver metastases after hepatectomy. Methods From 2002 to 2018, 611 patients with colorectal liver metastases (CRLM) who underwent hepatectomy at our center were reviewed. Primary tumors located from cecum to transverse colon were defined as right-sided group (n = 141); tumors located from splenic flexure to rectum were defined as left-sided group (n = 470). Patients were compared between two groups before and after a 1:1 propensity score analysis (PSM). Results Before PSM, median survival time and 5-year overall survival (OS) rate in right-sided group were 77 months and 56.3%, and those in left-sided group were 64 months and 51.1%, respectively. After PSM, median survival time and 5-year OS rate in right-sided group were 77 months and 55.9%, and those in left-sided group were 58.8 months and 47.3%, respectively. The OS rates did not differ between two groups before and after PSM (P = 0.575; P = 0.453). However, significant different recurrence free survival (RFS) rate was found before and after PSM between right-sided and left-sided group (P = 0.028, P = 0.003). Conclusions Primary tumor location of CRC impacts RFS for patients with liver metastases after resection. A more frequent follow up to detect early recurrence might be justified for CRLM patients with a right-sided CRC.

Background
Colorectal cancer (CRC) is the third most commonly diagnosed cancer worldwide.[1] In Asia, the incidence rate of CRC was rising.[2] Moreover, colorectal liver metastases (CRLM) present in nearly 20% of patients at the time of diagnosis and in approximately 60% of patients during the course of the disease.[3] Prognosis of CRLM patients remains dismaying, although progress has been made in surgical techniques and chemotherapy.[4] Many factors such as tumor size of liver metastases, tumor number and serum carcinoembryonic antigen (CEA) level are associated with outcomes in CRLM patients.[5] Primary tumor factors for instance lymph node status, pathology grade and genetic status may also influence the survival of
CRLM patients.[6, 7] Besides survival, genetic status of primary tumor were also found to predict resection margin and pathologic response in CRLM patients treated with neoadjuvant chemotherapy.[8, 9]

So far, many evidences demonstrated that patients with right-sided CRC tend to present with higher TNM stage, larger tumor size and worse outcomes than those with left-sided CRC.[10, 11] Some proposed that genetic differences may account for distinct carcinogenesis and biological behavior and lead to worse prognosis in right-sided CRC patients.[12, 13] However, whether patients with CRLM derived from right-sided CRC have worse prognosis than those derived from left-sided CRC remains controversial.[14, 15]

In this study, we aimed to explore the impact of primary tumor location of CRC on clinical characteristics and survival for CRLM patients after hepatectomy. Propensity score-matching (PSM) was used to strengthen causal arguments in observational study by reducing selection bias.

Methods
Study population
From July 2002 to March 2018, pathologically confirmed CRLM patients who underwent hepatectomy at Sun Yat-sen University Cancer center were identified from our database. To avoid the impact of different pathological type for prognosis, only pathological type of adenocarcinoma was included. All patients received primary tumor resection prior to or combined with hepatectomy. Exclusion criteria consisted of: Child-Pugh score of C, Eastern Cooperative Oncology Group-performance status (ECOG-PS) > 2, had double primary malignancies, lost in follow-up. A total of 611 patients were included in our study. According to the anatomical location, primary tumors located from cecum to transverse colon were defined as right-sided group (n = 141), and tumors located from splenic flexure to rectum were defined as left-sided group (n = 470).

Preoperative blood tests which included tumor markers were carried out within 2 weeks before resection of CRLM. Image to evaluate the resectability of liver metastases included magnetic resonance imaging (MRI) or computed tomography (CT). Intraoperative ultrasonography (US) was performed as conventional procedure to conduct radical resection of all tumors if possible. Definition
of R0 resection is resection of liver lesions with clear histological margins, and non R0 (R1/R2) resection is resection with histological positive margins or residual lesions in intra or extrahepatic. Overall survival (OS) was defined from the date of CRLM resection and to the date of death or lost to or last follow-up. Recurrence free survival (RFS) was defined as the interval from the date of R0 resection to the date of recurrence or death or last follow-up if without recurrence.

In all patients (n = 611), propensity score matching (PSM) was performed to reduce selection bias. Propensity scores were estimated using a logistic regression model based on age, gender, primary tumor lymph nodes status, time of liver metastases, preoperative CEA level, preoperative chemotherapy, number of liver metastases and size of largest liver lesions. A 1:1 balance ratio without replacement was performed using a 0.2 caliper width and the resulting score-matched pairs were used in subsequent analyses as indicated. This allowed us to generate 127 matched pairs from right-sided and left-sided groups.

Follow-ups
All patients were followed up monthly in the first 3 months, every 3 months in the first two years and every 3 to 6 months thereafter. Physical examination, blood tests, abdominal and pelvic US or CT/MRI were used for the surveillance of recurrence as appropriate.

Statistical analysis
Consecutive data were presented as mean (square deviation, SD). Independent-sample T-test, Chi-square test or Fisher’s exact test were used for analyzing the differences in clinicopathological characteristics between two groups as appropriate. The OS and RFS curves were constructed by Kaplan–Meier method and compared with the log-rank test. Cox proportional hazard regression model was performed to identify the hazard ratio (HR) of prognostic factors. A P value less than 0.05 was regarded as statistically significant. All statistical calculations were performed with IBM SPSS Statistics 25.0 software package (SPSS Inc., Chicago, IL).

Results
Clinicopathological characteristics
Of the 611 patients, 141 (23.1%) had primary tumors located in right-sided CRC, and 470 (76.9%) had primary tumors located in left-sided CRC. Clinicopathological characteristics of two groups were
presented in Table 1. Compared to left-sided group, right-sided group tended to have larger tumor size in CRC (4.2 vs. 3.6 cm, \(P = 0.011\)) and less people underwent preoperative chemotherapy before hepatectomy (48.2 vs. 61.1\%, \(P = 0.008\)). Other baseline parameters such as largest size of liver tumors, number and distribution of liver metastases were comparable between two groups.

**Table 1**

Baseline clinicopathological characteristics

| Characteristics                          | Before PSM (n = 611) | After PSM (n = 254) |
|-----------------------------------------|----------------------|---------------------|
|                                        | Right-sided group (n = 141) | Left-sided group (n = 470) | P-value |
|                                        | Right-sided group (n = 127) | Left-sided group (n = 127) | P-value |
| Mean age (± s.d.), years                | 57 (± 12)             | 55 (± 11)           | 0.313   | 56(± 12 )             | 54(± 12 )            | 0.381   |
| Gender, n (%)                           | 0.538                | 0.894               |         | 0.381                | 0.894               |         |
| Male                                    | 92 (65.2)            | 321 (68.3)          |         | 84(66.1)             | 86(67.7)            |         |
| Female                                  | 49 (34.8)            | 149 (31.7)          |         | 43(33.9)             | 41(32.3)            |         |
| Primary tumor characteristics            |                      |                     |         |                      |                     |         |
| Maximum tumor size, mean (± s.d.), cm   | 4.2 (± 2.3)          | 3.6 (± 2.2)         | 0.011*  | 4.2 (± 2.3)          | 3.7 (± 2.4)         | 0.048*  |
| T stage, n (%)                          | 0.592                | 0.807               |         | 0.807                | 0.807               |         |
| T1/T2                                   | 9 (7.1)              | 40 (9.2)            |         | 8(6.6)               | 10(8.2)             |         |
| T3/T4                                   | 118 (92.9)           | 433 (90.8)          | 0.546   | 114(93.4)            | 112(91.8)           | 0.363   |
| N stage, n (%)                          | 0.546                | 0.363               |         | 0.363                | 0.363               |         |
| N0                                      | 52 (39.7)            | 188 (43.0)          |         | 51(40.2)             | 43(33.9)            |         |
| N1/N2                                   | 79 (60.3)            | 249 (57.0)          |         | 76(59.8)             | 84(66.1)            |         |
| TNM stage, n (%)                        | 0.111                | 0.807               |         | 0.807                | 0.807               |         |
| I/II                                    | 9 (6.6)              | 53 (11.6)           |         | 8(6.6)               | 10(8.2)             |         |
| III/IV                                  | 127 (93.4)           | 404 (88.4)          |         | 114(93.4)            | 112(91.8)           |         |
| Postoperative chemotherapy, n (%)       |                      | 0.256               |         | 0.475                | 0.475               |         |
| Yes                                     | 103 (73.0)           | 366 (77.9)          |         | 91(71.7)             | 97(76.4)            |         |
| No                                      | 38 (27.0)            | 104 (22.1)          | 0.209   | 36(28.3)             | 30(23.6)            | 0.883   |
| CRLM characteristics                     |                      |                     |         |                      |                     |         |
| Presentation of CRLM, n (%)             | 0.209                | 0.883               |         | 0.883                | 0.883               |         |
| Synchronous                             | 37 (27.0)            | 150 (32.5)          |         | 31(24.4)             | 29(22.8)            |         |
| Metachronous                            | 100 (73.0)           | 305 (67.5)          |         | 96(75.6)             | 98(77.2)            |         |
| Preoperative chemotherapy, n (%)        |                      | 0.008*              |         | 0.900                | 0.900               |         |
| Yes                                     | 68 (48.2)            | 287 (61.1)          |         | 64(50.4)             | 62(48.8)            |         |
| No                                      | 73 (51.8)            | 183 (38.9)          | 0.755   | 63(49.6)             | 65(51.2)            |         |
| Preoperative CEA (µg/L), (> 200≤200) [n (%)] | 6/135 (4.3/95.7)     | 23/447 (4.9/95.1)   | 0.755   | 6/121 (4.7/95.3)     | 5/122 (3.9/96.1)    | 1.000   |
| Preoperative CA19-9 (kU/L), (> 35/ ≤35) [n (%)] | 30/110 (21.4/78.6)   | 97/370 (20.8/79.2)  | 0.867   | 26/100 (20.6/79.4)   | 24/103 (18.9/81.1)  | 0.754   |
| Tumor size (cm), median (IQR)           | 3.0 (2.0-4.5)        | 2.8 (1.6-4.0)       | 0.095   | 3.0 (1.8-4.0)        | 3.0 (1.5-4.0)       | 0.944   |
| Position, n (%)                         | 1.000                |                     |         | 1.000                |                     | 0.196   |
| Unilobar                                | 79 (56.4)            | 263 (56.6)          |         | 72(57.1)             | 81(65.3)            |         |
| Bilobar                                 | 82 (43.6)            | 308 (43.4)          |         | 82(42.9)             | 17(34.7)            |         |
| Number of tumor, n (%)       | 61 (43.6) | 202 (43.4) | 54 (42.9) | 43 (34.7) | 0.627 | 0.528 |
|----------------------------|-----------|------------|----------|----------|-------|-------|
| Multiple                   | 79 (56.0) | 275 (58.5) | 73 (57.5) | 67 (52.8) |       |       |
| Single                     | 62 (44.0) | 195 (41.5) | 54 (42.5) | 60 (47.2) |       |       |
| R0 resection, n (%)        |           |            | 1.000      |          |       | 0.886 |
| Yes                        | 119 (84.4)| 396 (84.4) | 106 (83.5)| 106 (84.1)|       |       |
| No                         | 22 (15.6) | 73 (15.6)  | 21 (15.6) | 20 (15.9) |       |       |
| CRS score, n (%)           |           |            | 0.538      |          |       | 0.922 |
| 1–2                        | 90 (64.7) | 312 (67.7) | 88 (71.0) | 88 (70.4) |       |       |
| 3–5                        | 49 (35.3) | 149 (32.3) | 36 (29.0) | 37 (29.6) |       |       |

IQR, inter-quartile range; T stage, tumor stage; N stage, node stage; CRLM, colorectal liver metastases; CEA, carcinoembryonic antigen; CA 19–9, carbohydrate antigen 19–9; R0 resection, hepatectomy on patients with clear histological margins; * P < 0.05.

Survival Analysis

The median OS for right-sided group and left-sided group were 77 months and 64 months respectively. The 1-, 3- and 5-year OS rates after CRLM resection in right-sided group were 91.0%, 75.0% and 56.3%, respectively, and 94.9%, 84.8%, and 51.1%, respectively, in left-sided group (P = 0.575; Fig. 1a). The 1-, 3- and 5-year RFS rates after R0 resection of liver metastases in right-sided group were 27.8%, 10.1%, and 5.1%, respectively, and 40.9%, 22.6%, and 8.8%, respectively, in left-sided group. Left-sided group have a significant better RFS rate than right-sided group (P = 0.028; Fig. 1b).

After PSM, the median OS time for patients in right-sided group was 77 months and was 58 months in left-sided group. Cumulative 1-, 3- and 5-year OS rates were 89.2%, 64.2% and 55.9%, respectively, in right-sided group, compared to 95.9%, 75.7% and 47.3%, respectively, in left-sided group (P = 0.453; Fig. 1c). The median RFS for patients in right-sided group was 5.8 months and was 10.9 months for patients in left-sided group. Cumulative 1- and 3-year RFS rates were 25.9% and 10.1%, respectively, in the patients from right-sided group, compared to 48.8% and 17.2%, respectively, in patients from left-sided group (P = 0.003; Fig. 1d).

Prognosis Stratified By Tumor Number And Crs Score

We further explored the prognostic role of CRC location according to CRS scores and liver lesions.

Similar OS were found in CRLM patients stratified by CRC location with different CRS scores.

Significant worse RFS were found in right-sided group before and after PSM among patients with different CRS scores (Fig. 2,3). Among patients with single liver lesion, OS and RFS were comparable before and after PSM between right-sided and left-sided group (P = 0.322, P = 0.338; P = 0.191, P = 0.118; Supplementary Fig. 1). Among patients with multiple liver metastases, significant worse RFS
were also found in right-sided group before and after PSM (P = 0.022, P = 0.012; Supplementary Fig. 2b,2d).

Prognostic Factors For Patients After Resection Of Liver Metastases

Next, we performed univariate and multivariate analysis to identify prognostic factors in our patients.

Before PSM, factors including lymph node metastases (HR 1.600, 95% confidence interval [CI] 1.155-2.216, P = 0.005), liver lesions > 5 cm (HR 1.923, 95% CI 1.298-2.849, P = 0.001) and non-R0 resection (HR 1.998, 95% CI 1.424–2.804, P < 0.001) were found to affect OS. After PSM, multivariate analysis identified that synchronous of liver metastases (HR 0.562, 95% CI 0.338-0.933, P = 0.026), liver lesions > 5 cm (HR 2.401, 95% CI 1.400-4.116, P = 0.001), multiple liver metastases (HR 1.917, 95% CI 1.092–3.367, P = 0.023) and non-R0 resection (HR 2.043, 95% CI 1.215–3.436, P = 0.007) were independent prognostic factors for OS (Table 2).

**Table 2**

Univariate and multivariate analysis for overall survival after liver metastases resection

| Characteristic | Before PSM (n = 611) | After PSM (n = 254) |
|----------------|----------------------|---------------------|
|                | Univariate analysis  | Multivariate analysis | Univariate analysis | Multivariate analysis |
|                | P-value | HR | 95%CI | P-value | HR | 95%CI | P-value |
| Age (year), (≤ 55 vs. >55) | 0.477 | 0.831 |
| Gender (male vs. female) | 0.785 | 0.759 |
| Tumor location Left-sided vs. right-sided | 0.575 | 0.453 |
| Primary tumor characteristics | | | |
| T stage (T3/T4 vs. T1/T2) | 0.201 | 0.605 |
| N stage (N1/N2 vs. N0) | 0.001 | 1.600 | 1.155-2.216 | 0.005 | 0.211 |
| Tumor size (cm), (> 4 vs. ≤4) | 0.254 | 0.668 |
| Postoperative chemotherapy (yes vs. no) | 0.501 | 0.317 |
| CRLM characteristics | | | |
| Presentation of CRLM (synchronous vs. asynchronous) | 0.766 | 0.031 | 0.562 | 0.338-0.933 | 0.026 |
| Characteristics                  | Before PSM (n = 515) | After PSM (n = 212) |
|---------------------------------|----------------------|---------------------|
|                                 | Univariate analysis  | Multivariate analysis | Univariate analysis | Multivariate analysis |
|                                 | P-value | HR      | 95%CI | P-value | P-value | HR      | 95%CI | P-value |
| Age (year), (≤ 55 vs. >55)      | 0.786    | 0.958   | 0.548–1.673 | 0.917 | 0.387–2.272 | 0.284 |
| Gender (male vs. female)        | 0.479    | 0.479   | 0.268–0.861 | 0.792 | 0.418–1.493 |
| Tumor size (cm), (>5 vs. ≤5)    | 0.001*   | 1.923   | 1.298–2.849 | <0.001* | 2.401 | 1.400–4.116 | 0.001* |
| Tumor number (multiple vs. single) | 0.001*  | 1.446   | 0.988–2.117 | <0.001* | 1.917 | 1.092–3.367 | 0.023* |
| Operative factors (plus ablation vs. resection only) | 0.001* | 1.723   | 1.129–2.630 | 0.012 | 0.015* | 1.690 | 0.880–3.245 | 0.115 |
| R0 resection (no vs. yes)       | 0.001*   | 1.998   | 1.424–2.804 | 0.001* | 0.002* | 2.043 | 1.215–3.436 | 0.007* |
| Postoperative chemotherapy (yes vs. no) | 0.057   | 0.083   | 0.001–0.527 | 0.614 |

HR, hazard ratio; CI, confidence interval; T stage, tumor stage; N stage, node stage; CRLM, colorectal liver metastases; CEA, carcinoembryonic antigen; CA 19–9, carbohydrate antigen 19–9; R0 resection, hepatectomy on patients with clear histological margins; * P < 0.05.

For RFS, significant factors in multivariate analysis before PSM were tumor location (HR 0.659, 95% CI 0.478–0.910, P = 0.011), lymph node metastases (HR 1.533, 95% CI 1.159–2.029, P = 0.003) and resection combined with ablation (HR 1.793, 95% CI 1.253–2.566, P = 0.001). After PSM, only tumor location (HR 0.593, 95% CI 0.387–0.911, P = 0.017) was independent prognostic factor for RFS on multivariate analysis (Table 3).
| Tumor location | 0.029* | 0.659 | 0.478–0.910 | 0.011* | 0.004* | 0.593 | 0.387–0.911 | 0.017* |
|----------------|-------|-------|-------------|--------|--------|-------|-------------|--------|
| Left-sided vs. right-sided | 0.219 | 0.798 |
| Primary tumor characteristics | 0.003* | 1.533 | 1.159–2.029 | 0.003* | 0.728 |
| T stage (T3/T4 vs. T1/T2) | 0.628 | 0.898 |
| N stage (N1/N2 vs. N0) | 0.018* | 1.417 | 0.944–2.217 | 0.093 | 0.020* | 1.141 | 0.650–2.006 | 0.645 |
| Tumor size (cm), (> 4 vs. ≤ 4) | 0.001* | 1.355 | 0.975–1.884 | 0.070 | 0.003* | 1.535 | 0.943–2.498 | 0.085 |
| Postoperative chemotherapy (yes vs. no) | 0.056 | 0.526 |
| CEA (µg/L), (> 200 vs. ≤ 200) | 0.748 | 0.899 |
| CA19-9 (kU/L), (> 35 vs. ≤ 35) | 0.315 | 0.274 |
| Tumor size (cm), (> 5 vs. ≤ 5) | 0.001* | 1.244 | 0.907–1.706 | 0.176 | 0.001* | 1.539 | 0.958–2.474 | 0.075 |
| Tumor number (multiple vs. single) | 0.001* | 1.793 | 1.253–2.566 | 0.001* | 0.034* | 1.324 | 0.742–2.363 | 0.342 |
| Operative factors (plus ablation vs. resection only) | 0.319 | 0.020* | 1.392 | 0.789–2.458 | 0.254 |
| Postoperative chemotherapy (yes vs. no) | 0.001* | 1.244 | 0.907–1.706 | 0.176 | 0.001* | 1.539 | 0.958–2.474 | 0.075 |
| R0 resection, hepatectomy on patients with clear histological margins; HR, hazard ratio; CI, confidence interval; T stage, tumor stage; N stage, node stage; CRLM, colorectal liver metastases; CEA, carcinoembryonic antigen; CA 19–9, carbohydrate antigen 19–9; * P < 0.05. |

**Discussion**

Many clinicopathological factors and molecular features affect survival of CRC patients. [16] Among
them, primary tumor location of CRC is a notable factor which can affect outcomes of patients.[17] So far, many evidence have revealed that right-sided CRC patients have poorer prognosis than left-sided CRC patients.[18] Differences in RAS status, microsatellite instability (MSI) and CpG island methylator (CIMP) phenotype may account for diverse clinicopathological characteristics and outcomes between right-sided and left-sided CRC patients.[19]

Recently, data from two pooled studies have shown that OS, progress free survival and objective response rate were much worse among unresectable CRLM patients with right-sided tumor than those with left-sided tumor.[20, 21] However, whether primary tumor location of CRC affects prognosis of CRLM patients after hepatectomy remains debatable. One study found CRLM patients with left-sided CRC have worse disease free survival but better OS after liver resection, as authors suggested that tumors of patients with right-sided CRC relapsed less frequently than left-sided patients, but they had more aggressive disease once they recurred.[22] A meta-analysis concluded that CRLM patients with right-sided CRC had worse OS than those with left-sided CRC.[15] It should be noted that this analysis included nine non-Asian countries and only three studies from Asian countries. Some other studies showed that primary tumor location did not influence prognosis of CRLM patients after hepatectomy. [23–25] In CRLM patients after microwave ablation, comparable outcomes were also observed between right-sided group and left-sided group.[26, 27]

In our study, significant worse RFS was found in right-sided group patients even when the comparison groups are balanced with respect to potential prognostic factors. Further analysis in patients before and after PSM also revealed that primary location of CRC was a prognostic factor for RFS. However, OS was comparable between 2 groups. Based on these data, we think that the disparity between the results of RFS and OS may be due to benefit of subsequent therapies after recurrence. Tumors may recur more frequently in CRLM patients with right-sided CRC, but efficient and multi-discipline therapies to treat recurrence lesions may result in comparable prognosis.

The inconsistent effects of primary tumor location in different studies may be partially explained by following reasons. Firstly, right-sided CRC were more characterized by high MSI (MSI-H) and high CIMP, which may lead to poor response to chemotherapy.[28] Therefore, compared to left-sided CRC,
there may be more unresectable liver metastases from right-sided CRC. These unresectable patients may contribute to poorer OS of right-sided CRC than left-sided CRC. Secondly, since resection of liver metastases is the potentially curative approach for CRLM patients, the benefits of hepatectomy may neutralize the prognostic effect of primary tumor location for CRLM patients.[24, 25] Thirdly, the prognostic value of primary tumor location may depends on tumor stages. There were evidences that survival was not affected by tumor location in early stage CRC patient while it was influenced in patients with advanced unresectable CRLM.[18, 29, 30] Moreover, difference in ethnicity may also contribute to the discrepancy in result. Therefore, the prognostic value of tumor location needs further prospective investigation.

It is important to note the limitations in our study. Although PSM was used to reduce selection bias caused by retrospective design, our study only had limited number of patients in a single institution. Furthermore, genetic information such as RAS type and BRAF type were not available in most of our patients. We were unable to assess the prognostic impact of genetic status in two groups. Hence, future studies which include multicenter, large scale of patients with genetic data are needed to confirm our conclusion.

**Conclusion**

Primary tumor location of CRC impacts RFS for patients after resection of liver metastases. A more frequent follow up to detect early recurrence might be justified for CRLM patients with a right-sided primary tumor location.

**Abbreviations**

CRC: colorectal cancer; CRLM: colorectal liver metastases; PSM: propensity score analysis; OS: overall survival; RFS: recurrence free survival; CEA: carcinoembryonic antigen; ECOG-PS: Eastern Cooperative Oncology Group-performance status; MRI: magnetic resonance imaging; CT: computed tomography; US: ultrasonography; HR: hazard ratio; CI: confidence interval; MSI: microsatellite instability; CIMP: CpG island methylator;

**Declarations**

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Authors’ contributions

BKL and YYF contributed to the research design; YPZ, YJW, YCY, JLQ, YXQ, WH, YZ, ZQW, ZZP, DSW, YHL, ZHL, GC, PRD, XJW and YKG contributed to the data collection, data analysis, and manuscript writing. YPZ, YJW, YCY, YZ and JLQ contributed to the data collection and manuscript writing. All authors contributed to the writing review and editing. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Ethical approval was waived by the Sun Yat-sen University Cancer Centre in view of the retrospective nature of the study and all the procedures being performed were part of the routine care. This study was performed in accordance with the Helsinki Declaration of 1975.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Supplementary Figure Legends

**Supplementary Figure 1.** (a) Overall survival and (b) recurrence free survival in CRLM patients stratified by CRC location with single liver lesion. (c) Overall survival and (d) recurrence free survival in CRLM patients stratified by CRC location with single liver lesion after PSM.

**Supplementary Figure 2.** (a) Overall survival and (b) recurrence free survival in CRLM patients stratified by CRC location with multiple liver lesions. (c) Overall survival and (d) recurrence free survival in CRLM patients stratified by CRC location with multiple liver lesions after PSM.

Figures
Figure 1

(a) Overall survival (b) recurrence free survival in CRLM patients stratified by CRC location.

(c) Overall survival and (d) recurrence free survival in CRLM patients stratified by CRC location after PSM.
Figure 2

(a) Overall survival and (b) recurrence free survival in CRLM patients stratified by CRC location with low CRS scores (score ≤ 2). (c) Overall survival and (d) recurrence free survival in CRLM patients stratified by CRC location with low CRS scores after PSM.
Figure 3

(a) Overall survival and (b) recurrence free survival in CRLM patients stratified by CRC location with high CRS scores (score ≥ 2). (c) Overall survival and (d) recurrence free survival in CRLM patients stratified by CRC location with high CRS scores after PSM.

Supplementary Files

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