ISSN 2307-8960 (online)

World Journal of *Clinical Cases*

World J Clin Cases 2020 August 6; 8(15): 3136-3376

Published by Baishideng Publishing Group Inc

World Journal of Clinical Cases

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Semimonthly Volume 8 Number 15 August 6, 2020

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ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Dr. Romano is Professor of Medicine-Gastroenterology at the University of Campania "Luigi Vanvitelli" in Naples, Italy. Dr. Romano received his MD degree cum Laude at the University Federico II in Naples, Italy in 1980 and, after 4 year of Post-Graduate course, he became Specialist in Gastroenterology and Gastrointestinal Endoscopy. Dr. Romano's research interest was on the cross-talk between H. pylori and gastric epithelial cells, and presently is mainly focused on H. pylori eradication therapy and on the role of nutraceuticals in gastrointestinal diseases. Dr. Romano is presently the Chief of the Endoscopy and Chronic Inflammatory Gastrointestinal Disorders Unit, and Teacher at the University of Campania "Luigi Vanvitelli" in Naples, Italy.

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RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL
World Journal of Clinical Cases

ISSN
ISSN 2307-8960 (online)

LAUNCH DATE
April 16, 2013

FREQUENCY
Semimonthly

EDITORS-IN-CHIEF
Dennis A Bloomfield, Sandro Vento, Bao-Gan Peng

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PUBLICATION DATE
August 6, 2020

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World J Clin Cases 2020 August 6; 8(15): 3230-3239

DOI: 10.12998/wjcc.v8.i15.3230

ISSN 2307-8960 (online)

ORIGINAL ARTICLE

Retrospective Study

Colorectal adenocarcinoma patients with M1a diseases gain more clinical benefits from palliative primary tumor resection than those with M1b diseases: A propensity score matching analysis

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Author contributions: Li CL and Zhao JQ designed the research and critically revised the manuscript for important intellectual content; all authors performed the research, analyzed the data, and wrote the paper.

Institutional review board statement: The study was approved by the Bioethics Committee of the Affiliated Huaian No. 1 People's Hospital of Nanjing Medical University, China.

Informed consent statement: All patients from the SEER database have agreed to participate in scientific research.

Conflict-of-interest statement: All authors declare no competing financial interests.

Data sharing statement: No additional data are available.

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Abstract

BACKGROUND

Surgical resection is regarded as the only potentially curative treatment option for patients with metastatic colorectal cancer (CRC). The National Comprehensive Cancer Network clinical practice guidelines do not recommend palliative surgery unless there is a risk of severe symptoms. However, accumulating evidence has shown that palliative surgery is associated with more favorable outcomes for patients with metastatic CRC.

AIM

To investigate the separate role of palliative primary tumor resection for patients with stage IVA (M1a diseases) and stage IVB (M1b diseases) colorectal adenocarcinoma (CRA).

METHODS

CRA patients diagnosed from 2010 to 2015 with definite M1a and M1b categories according to the 8th edition of American Joint Committee on Cancer staging system were selected from the Surveillance Epidemiology and End Results (SEER) database. To minimize potential selection bias, the data were adjusted by propensity score matching (PSM). Baseline characteristics, including gender, year of diagnosis, age, marital status, primary site, surgical information, race, grade, chemotherapy, and radiotherapy, were recorded and analyzed. Univariate and multivariate analyses were performed to explore the separate role of palliative surgery for patients with M1a and M1b diseases.

RESULTS

A total of 19680 patients with metastatic CRA were collected from the SEER database, including 10399 cases of M1a diseases and 9281 cases of M1b diseases.

Manuscript source: Unsolicited manuscript

Received: January 14, 2020
Peer-review started: January 14, 2020
First decision: April 12, 2020
Revised: April 25, 2020
Accepted: June 29, 2020
Article in press: June 29, 2020
Published online: August 6, 2020

P-Reviewer: Akbulut S, Lee CL, Nakano H
S-Editor: Dou Y
L-Editor: Wang TQ
E-Editor: Li JH

Common independent prognostic factors for both M1a and M1b patients included year of diagnosis, age, race, marital status, primary site, grade, surgery, and chemotherapy. After PSM adjustment, 3732 and 3568 matched patients in the M1a and M1b groups were included, respectively. Patients receiving palliative primary tumor resection had longer survival time than those without surgery ($P < 0.001$). For patients with M1a diseases, palliative resection could increase the median survival time by 9 mo; for patients with M1b diseases, palliative resection could prolong the median survival time by 7 mo. For M1a diseases, patients with lung metastasis had more clinical benefit from palliative resection than those with liver metastasis (15 mo for lung metastasis *vs* 8 mo for liver metastasis, $P < 0.001$).

CONCLUSION
CRA patients with M1a diseases gain more clinical benefits from palliative primary tumor resection than those with M1b diseases. Those patients with M1a (lung metastasis) have superior long-term outcomes after palliative primary tumor resection.

Key words: Colorectal adenocarcinoma; Palliative primary tumor resection; Distant metastasis; Propensity score matching; Surveillance Epidemiology and End Results; Overall survival

Core tip: The National Comprehensive Cancer Network clinical practice guidelines do not recommend palliative surgery for metastatic colorectal adenocarcinoma (CRA). Using the Surveillance Epidemiology and End Results database, we found that patients with M1a diseases had a significant survival benefit compared to those with M1b diseases and patients with M1a (lung metastasis) got best long-term outcomes with median overall survival prolonged by 15 mo compared with those without surgical treatment. These findings provide further evidence to support the use of palliative surgical procedure to treat metastatic CRA and develop effective individualized treatment strategy.

Citation: Li CL, Tang DR, Ji J, Zang B, Chen C, Zhao JQ. Colorectal adenocarcinoma patients with M1a diseases gain more clinical benefits from palliative primary tumor resection than those with M1b diseases: A propensity score matching analysis. *World J Clin Cases* 2020; 8(15): 3230-3239
URL: https://www.wjgnet.com/2307-8960/full/v8/i15/3230.htm
DOI: https://dx.doi.org/10.12998/wjcc.v8.i15.3230

INTRODUCTION

Colorectal cancer (CRC) is one of the three most common malignancies with 135430 individuals expected to be diagnosed in 2017 in the United States[1]. However, approximately 20% of new CRC patients are diagnosed with distant-stage tumors, resulting in poor long-term outcomes with a 5-year survival rate of 23.2%[2].

Surgical resection is regarded as the only potentially curative treatment option for this disease and could significantly improve the prognosis of patients with metastatic CRC[3]. Rees *et al*[4] reported that the 5-year cancer-specific survival (CSS) rate for metastatic CRC patients undergoing primary and hepatic resection was 36%. Abdalla *et al*[5] showed that patients receiving surgical resection of primary tumors and liver metastases had a 5-year survival rate of up to 58%. Similarly, curative surgical treatment could increase the 5-year survival rate of 32% to 68% in CRC patients with resectable lung metastasis[6,7]. Unfortunately, only one-fifth to one-quarter of metastatic CRC patients can receive curative surgical treatment[8], indicating that metastatic CRC patients are a heterogenous population.

According to the 8th edition of American Joint Committee on Cancer (AJCC) tumor-node-metastasis staging system, metastatic CRC are classified into M1a (metastasis confined to one organ or site) and M1b (metastases in more than one organ/site or the peritoneum). Complete resection is impossible for most metastatic CRC patients (especially for those with M1b diseases) even after neoadjuvant chemoradiation. The

National Comprehensive Cancer Network clinical practice guidelines[9] do not recommend palliative surgery unless there is a risk of significant acute bleeding, obstruction, perforation, or other severe symptoms based on comprehensive analysis of the literature[10-12]. However, accumulating evidence has shown that palliative surgery is associated with more favorable outcomes. For example, a pooled analysis including four randomized trials reported that patients receiving palliative primary tumor removal had prolonged overall survival (OS) compared with those not receiving operation[13]. Another population-based retrospective study reviewing 37793 metastatic CRC patients showed that palliative surgery was significantly related to better OS and CSS[14]. Finally, a systematic review consisting of 21 studies indicated that there was a survival benefit for palliative surgery in patients with metastatic CRC and criteria for palliative surgery should be extended on the basis of World Health Organization (WHO) performance status (PS) or tumor burden[15].

However, to our best knowledge, no studies have classified stage IV into subsets to assess the role of palliative surgery. Adenocarcinoma is the most common pathological type of CRC, accounting for approximately 90% of cases[16]. Thus, we subdivided colorectal adenocarcinoma (CRA) patient populations with stage IV disease on the basis of comorbidities from the Surveillance, Epidemiology, and End Results (SEER) database into stage IVA (M1a diseases) and stage IVB (M1b diseases). Outcomes of palliative surgery were then independently assessed.

MATERIALS AND METHODS

Patient source

Patient data, originating between 2010 and 2015, was collected from the SEER database, one of the largest cancer databases in the world[14]. The selection criteria were as follows: (1) Patients 18 years old or older; (2) Disease histologically diagnosed as adenocarcinoma; (3) Treated for first primary tumor; (4) Definite M1a or M1b diseases according to the 8th edition of AJCC staging system; (5) No surgery for metastatic sites (including distant lymph nodes); (6) Surgical procedure or no surgical procedure to primary tumor (excluding tumor destruction or no pathologic specimen or unknown whether there was a pathologic specimen); and (7) Active follow-up. Cases with unknown survival time, status, or those coded as 0 mo were excluded. The entire cohort was divided into two groups based on the median age and calculation result of X-tile program (Yale University, 3.6.1, Supplementary Figure 1). After propensity score matching (PSM), 2935 patients with M1a diseases and 2145 patients with M1b diseases were excluded owing to a lack of counterpart propensity scores. In survival analysis for M1a (liver metastasis) and M1a (lung metastasis), 2202 and 267 patients were further excluded, respectively. Follow-up time ranged from 1 to 71 mo.

Statistical analyses

Baseline characteristics of metastatic CRA patients, including sex, year of diagnosis, age, marital status, primary site, surgical information, race, grade, chemotherapy, and radiotherapy, were recorded and analyzed by χ^2 test. The patient prognosis was assessed using univariate and multivariate Cox regression analyses with hazard ratios and 95% confidence intervals. To minimize potential selection bias, 1:1 PSM without replacement was used to investigate the effect of palliative primary tumor resection on metastatic CRA. After PSM adjustment, Kaplan-Meier method was employed to analyze the OS for M1a and M1b patients. All statistical analyses were conducted using IBM SPSS Statistics 22.0. P values < 0.05 were considered statistically significant.

RESULTS

Baseline characteristics

A total of 19680 patients with metastatic CRA were collected from the SEER database, which included 10399 cases of M1a diseases and 9281 cases of M1b diseases (Table 1). The entire cohort consisted of 11107 (56.4%) males and 8573 (43.6%) females with a median age of 63 years (ranging from 18 to 108). Most patients were of White ethnicity (74.8%) and more than half of them had well or moderately differentiated tumors (grade I + II). Next, 15476 (78.6%) cases of primary tumors were located in the colon and 4204 (21.4%) in the rectum. The prevalence of metastatic CRA between 2010 and 2012 was similar to that between 2013 and 2015. However, M1b diseases seemed to

Table 1 Baseline characteristics of metastatic colorectal adenocarcinoma patients

Variable	Total (*n* = 19680) (%)	M1a (*n* = 10399) (%)	M1b (*n* = 9281) (%)	*P* value[1]
Gender				
Female	8573 (43.6)	4462 (42.9)	4111 (44.3)	0.050
Male	11107 (56.4)	5937 (57.1)	5170 (55.7)	
Year of diagnosis				< 0.001
2010-2012	9835 (50.0)	5342 (51.4)	4493 (48.4)	
2013-2015	9845 (50.0)	5057 (48.6)	4788 (51.6)	
Age (years)				< 0.001
< 65	10680 (54.3)	5507 (53.0)	5173 (55.7)	
≥ 65	9000 (45.7)	4892 (47.0)	4108 (44.3)	
Race				0.011
White	14715 (74.8)	7856 (75.5)	6859 (73.9)	
Black	3033 (15.4)	1578 (15.2)	1455 (15.7)	
Others	1932 (9.8)	965 (9.3)	967 (10.4)	
Marital status				0.661
Married	9774 (49.7)	5180 (49.8)	4594 (49.5)	
Others	9906 (50.3)	5219 (50.2)	4687 (50.5)	
Primary site				0.027
Colon	15476 (78.6)	8114 (78.0)	7362 (79.3)	
Rectum	4204 (21.4)	2285 (22.0)	1919 (20.7)	
Grade				< 0.001
I + II[2]	11321 (57.5)	6525 (62.7)	4796 (51.7)	
III + IV[3]	3889 (19.8)	1909 (18.4)	1980 (21.3)	
Others	4470 (22.7)	1965 (18.9)	2505 (27.0)	
Surgery				< 0.001
Yes	9360 (47.6)	5787 (55.6)	3573 (38.5)	
No	10320 (52.4)	4612 (44.4)	5708 (61.5)	
Chemotherapy				0.415
Yes	14057 (71.4)	7402 (71.2)	6655 (71.7)	
No/unknown	5623 (28.6)	2997 (28.8)	2626 (28.3)	
Radiotherapy				
Yes	975 (5.0)	670 (6.4)	305 (3.3)	< 0.001
No	18705 (95.0)	9729 (93.6)	8976 (96.7)	

[1]χ^2 test.
[2]Well or moderately differentiated tumors.
[3]Poorly differentiated or undifferentiated tumors.

account for a larger proportion from 48.4% during 2010-2012 to 51.6% during 2013-2015 while M1a diseases showed the opposite prevalence trend.

Of the entire cohort, 14057 (71.4%) metastatic CRA patients received chemotherapy and 975 (5.0%) received radiotherapy; 9360 (47.6%) metastatic CRA patients received palliative primary tumor resection while 10320 (52.4%) did not. The proportion of patients with M1a diseases undergoing surgical procedure was much higher than that of M1b diseases (55.6% for M1a and 38.5% for M1b).

Survival analysis

Univariate and multivariate Cox regression analyses for OS for both M1a and M1b patients were performed (Table 2). The common independent prognostic factors in both M1a and M1b patients included year of diagnosis (2010-2012 *vs* 2013-2015), age (< 65 *vs* ≥ 65), race (white *vs* black), marital status (married *vs* others), primary site (colon *vs* rectum), grade (I + II *vs* III + IV), surgery (yes *vs* no), and chemotherapy (yes *vs* no/unknown). Radiotherapy (yes *vs* no) was an independent prognostic factor for M1a patients but not for M1b patients.

After PSM adjustment, we obtained 3732 and 3568 matched patients in the M1a and M1b groups, respectively. Their survival curves were plotted by the Kaplan-Meier method (Figure 1A and D). Patients receiving palliative primary tumor resection had longer survival time than those without surgery ($P < 0.001$). For patients with M1a diseases, palliative resection could increase the median survival time by 9 mo; for patients with M1b diseases, palliative resection can prolong the median survival time by 7 mo (Table 3). Then M1a diseases were further subdivided by metastatic site. Patients with liver metastasis and lung metastasis were included in the further analysis, whereas patients with bone metastasis and brain metastasis were excluded because of small sample size. As shown in Figure 1B and C, patients with lung metastasis could obtain more clinical benefit from palliative resection than those with liver metastasis (15 mo for lung metastasis *vs* 8 mo for liver metastasis, Table 3, $P < 0.001$).

DISCUSSION

Metastatic CRC is a lethal disease with a poor prognosis. While patients with metastatic CRC can obtain clinical benefits from curative surgery, there is still controversy with respect to the role of palliative primary tumor resection. To the best of our knowledge, this is the first population-based study subdividing stage IV into stages IVA (M1a diseases) and IVB (M1b diseases) to evaluate the effect of palliative primary tumor resection. It was determined that patients with M1a diseases could obtain more survival benefits than those with M1b diseases and patients with M1a (lung metastasis) got best long-term outcomes with median OS prolonged by 15 mo compared with those without surgical treatment. These findings provided further evidence to support palliative surgical procedure to metastatic CRA and develop effective individualized treatment strategy.

There were many predictors of OS in patients with unresectable metastatic CRC, including WHO PS, carcinoembryonic antigen level, number of metastatic sites, and palliative surgery[13]. Li *et al*[17] showed that tumor location (right colon *vs* left colon *vs* rectum) was also an independent prognostic factor for metastatic CRC. The results were in line with our findings that patients with rectal cancer were at a lower risk of death than those with colon cancer, possibly owing to higher proportion of lung metastasis in patients with rectal cancer[18]. However, no studies focus on the effect of palliative surgery according to the number of metastatic sites or organs (M1a or M1b). Tarantino *et al*[14] reported that the survival difference between patients with palliative resection and those without palliative resection was anticipated to decrease due to the development of chemotherapeutic and molecule-targeted drugs. Actually, the significance of survival difference has persisted over time. This may be explained by the heterogeneity of stage IVA (M1a diseases) and stage IVB (M1b diseases). The development of systemic treatment could decrease the survival difference and increase surgery conversion indeed. The proportion of M1b diseases grew from 48.6% during 2010-2012 to 51.6% during 2013-2015 (Table 1, $P < 0.001$) and such patients were less likely to undergo surgical treatment than those with M1a diseases. This may also explain the decreased rate of patients undergoing primary tumor removal observed during 1998-2009 in Tarantino's study[14].

Liver and lung metastases are the most two common distant metastases from CRC[7], accounting for 50% and 10%-15% of CRC, respectively[19,20]. The prognosis of patients with liver or lung metastasis is usually better than those with brain or bone metastasis[21]. According to the published literature, median OS was 3-6 mo for patients with brain metastases and 5-7 mo for those with bone metastases[22-28]. For patients with unresectable liver metastases who were treated with chemotherapy only, median OS was approximately 20 mo[29]. By comparison, patients with unresectable lung metastases, who achieved a complete or partial response to chemotherapy, could achieve a median OS of 27 mo[30]. From the perspective of epidemiology, the median time between the diagnosis of CRC and the emergence of liver metastases was shorter

Table 2 Univariate and multivariate cox regression analyses for overall survival of metastatic colorectal adenocarcinoma patients

	M1a				M1b			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	HR (95%CI)	*P* value	HR (95%CI)	*P* value	HR (95%CI)	*P* value	HR (95%CI)	*P* value
Gender								
Female	Reference		Reference		Reference		Reference	
Male	1.100 (1.054-1.147)	< 0.001	1.025 (0.975-1.077)	0.339	1.043 (1.002-1.086)	0.042	1.020 (0.972-1.070)	0.428
Year of diagnosis								
2010-2012	Reference		Reference		Reference		Reference	
2013-2015	0.972 (0.929-1.016)	0.208	0.981 (0.929-1.036)	0.486	0.965 (0.925-1.006)	0.096	0.972 (0.924-1.023)	0.277
Age (years)								
< 65	Reference		Reference		Reference		Reference	
≥ 65	1.675 (1.606-1.746)	< 0.001	1.413 (1.344-1.485)	< 0.001	1.527 (1.466-1.589)	< 0.001	1.319 (1.256-1.385)	< 0.001
Race								
White	Reference		Reference		Reference		Reference	
Black	1.138 (1.075-1.206)	< 0.001	1.114 (1.042-1.192)	0.002	1.127 (1.068-1.191)	< 0.001	1.137 (1.064-1.215)	< 0.001
Others	0.910 (0.844-0.981)	0.013	0.864 (0.792-0.942)	0.001	0.953 (0.891-1.020)	0.164	0.952 (0.878-1.031)	0.227
Marital status								
Married	Reference		Reference		Reference		Reference	
Others	1.326 (1.272-1.383)	< 0.001	1.142 (1.086-1.201)	< 0.001	1.212 (1.165-1.262)	< 0.001	1.078 (1.026-1.132)	0.003
Primary site								
Colon	Reference		Reference		Reference		Reference	
Rectum	0.799 (0.758-0.841)	< 0.001	0.759 (0.711-0.811)	< 0.001	0.839 (0.797-0.882)	< 0.001	0.779 (0.731-0.830)	< 0.001
Grade								
I + II	Reference		Reference		Reference		Reference	
III + IV	1.530 (1.450-1.614)	< 0.001	1.580 (1.484-1.682)	< 0.001	1.447 (1.375-1.523)	< 0.001	1.506 (1.417-1.601)	< 0.001
Others	1.702 (1.614-1.795)	< 0.001	1.149 (1.074-1.228)	< 0.001	1.544 (1.473-1.619)	< 0.001	1.178 (1.109-1.251)	< 0.001
Surgery								
Yes	Reference		Reference		Reference		Reference	
No	1.953 (1.859-2.051)	< 0.001	2.133 (2.011-2.262)	< 0.001	1.632 (1.552-1.716)	< 0.001	1.955 (1.843-2.074)	< 0.001
Chemotherapy								
Yes	Reference		Reference		Reference		Reference	
No/unknown	2.520 (2.395-2.651)	< 0.001	2.282 (2.164-2.405)	< 0.001	2.558 (2.430-2.692)	< 0.001	2.565 (2.432-2.705)	< 0.001
Radiotherapy								
Yes	Reference		Reference		Reference		Reference	
No	2.337 (2.069-2.639)	< 0.001	1.236 (1.085-1.408)	0.001	1.695 (1.465-1.961)	< 0.001	0.946 (0.813-1.101)	0.472

HR: Hazard ratio; CI: Confidence interval.

than that for lung metastases (17.2 mo for liver *vs* 24.6 mo for lung)[31], which indicated that liver metastases possessed more aggressive malignant behavior to some extent. These survival findings were similar to the present results (22 mo for liver metastasis with palliative surgery *vs* 33 mo for lung metastasis with palliative surgery).

There are several limitations to this study that should be noted. PSM can adjust potential confounding variables and decrease selection bias as much as possible, increasing precision by creating a 'quasi-randomized' experiment[32]. However, we

Table 3 Survival time for metastatic colorectal adenocarcinoma patients with or without palliative primary tumor resection

	Median survival time (95%CI)	1-yr survival rate (%)	3-yr survival rate (%)
M1a (total)			
No surgery	14 (13.275-14.725)	54.4	13.9
Surgery	23 (21.977-24.023)	70.4	32.6
M1a (liver metastasis)			
No surgery	14 (13.320-14.780)	53.8	13.4
Surgery	22 (20.955-23.045)	69.2	29.8
M1a (lung metastasis)			
No surgery	18 (15.692-20.308)	62.2	18.6
Surgery	33 (28.014-37.986)	77.5	45.4
M1b			
No surgery	10 (9.401-10.599)	42.2	8.6
Surgery	17 (16.209-17.791)	60.0	20.4

would like to acknowledge the limitations of our study. First, some significant factors such as surgical complications, life quality, operative tolerance, and laboratory parameters were not included. Second, detailed number of metastases in a single organ was not provided in the SEER database, which hampered further analysis for M1a diseases. Third, further classifications for M1 category in the AJCC staging system were not recorded before 2010, and only patient data between 2010 and 2015 were collected. The conclusions should be validated by more prospective data in the future.

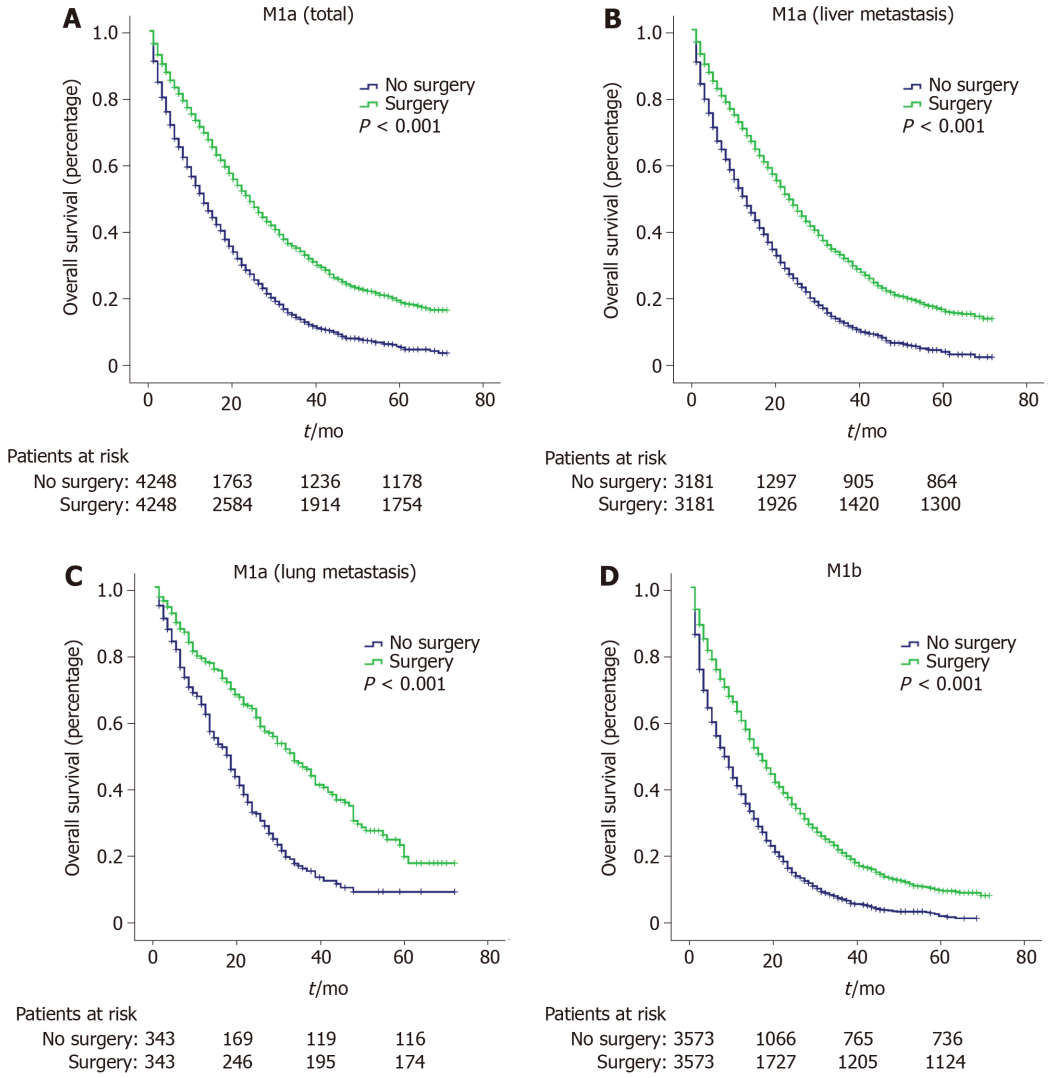

Figure 1 Survival time for metastatic colorectal adenocarcinoma patients with or without palliative primary tumor resection. A: Total patients with M1a diseases; B: Patients with M1a diseases (liver metastasis); C: Patients with M1a diseases (lung metastasis); D: Patients with M1b diseases.

ARTICLE HIGHLIGHTS

Research background

The National Comprehensive Cancer Network clinical practice guidelines do not recommend palliative surgery for metastatic colorectal adenocarcinoma (CRA) unless there is a risk of significant acute bleeding, obstruction, perforation, or another severe symptom.

Research motivation

Accumulating evidence has demonstrated that palliative surgery for metastatic CRA patients was associated with more favorable outcomes. However, no studies further classified CRA patients with stage IV into subsets to assess the role of palliative surgery.

Research objectives

The purpose of this study was to investigate the separate role of palliative primary tumor resection for CRA patients with stage IVA (M1a diseases) and stage IVB (M1b diseases).

Research methods

CRA patient records with definite M1a and M1b categories were analyzed by adjusted propensity score matching. Patient prognosis was assessed by univariate and

multivariate Cox regression analyses with hazard ratios and 95% confidence intervals.

Research results

Patients with metastatic CRA receiving palliative primary tumor resection had a longer survival time than those who did not ($P < 0.001$). Palliative resection increased the median survival time by 9 mo and by 7 mo for patients with M1a and M1b diseases, respectively. For M1a diseases, patients with lung metastasis had more survival benefit from palliative resection than those with liver metastasis (15 mo for lung metastasis *vs* 8 mo for liver metastasis, $P < 0.001$).

Research conclusions

Palliative primary tumor resection improves survival for all CRA patients but more beneficial for those with M1a diseases than those with M1b diseases. Specifically, patients with M1a (lung metastasis) had the best long-term outcomes after palliative primary tumor resection.

Research perspectives

These findings provided further evidence to support the use of palliative surgical procedures to treat metastatic CRA and develop effective individualized treatment strategies.

REFERENCES

1 **Siegel RL**, Miller KD, Jemal A. Cancer Statistics, 2017. *CA Cancer J Clin* 2017; **67**: 7-30 [PMID: 28055103 DOI: 10.3322/caac.21387]

2 **Zhang J**, Gong Z, Gong Y, Guo W. Development and validation of nomograms for prediction of overall survival and cancer-specific survival of patients with Stage IV colorectal cancer. *Jpn J Clin Oncol* 2019; **49**: 438-446 [PMID: 30924498 DOI: 10.1093/jjco/hyz035]

3 **Tomasello G**, Petrelli F, Ghidini M, Russo A, Passalacqua R, Barni S. FOLFOXIRI Plus Bevacizumab as Conversion Therapy for Patients With Initially Unresectable Metastatic Colorectal Cancer: A Systematic Review and Pooled Analysis. *JAMA Oncol* 2017; **3**: e170278 [PMID: 28542671 DOI: 10.1001/jamaoncol.2017.0278]

4 **Rees M**, Tekkis PP, Welsh FK, O'Rourke T, John TG. Evaluation of long-term survival after hepatic resection for metastatic colorectal cancer: a multifactorial model of 929 patients. *Ann Surg* 2008; **247**: 125-135 [PMID: 18156932 DOI: 10.1097/SLA.0b013e31815aa2c2]

5 **Abdalla EK**, Vauthey JN, Ellis LM, Ellis V, Pollock R, Broglio KR, Hess K, Curley SA. Recurrence and outcomes following hepatic resection, radiofrequency ablation, and combined resection/ablation for colorectal liver metastases. *Ann Surg* 2004; **239**: 818-25; discussion 825-7 [PMID: 15166961 DOI: 10.1097/01.sla.0000128305.90650.71]

6 **Riquet M**, Foucault C, Cazes A, Mitry E, Dujon A, Le Pimpec Barthes F, Médioni J, Rougier P. Pulmonary resection for metastases of colorectal adenocarcinoma. *Ann Thorac Surg* 2010; **89**: 375-380 [PMID: 20103301 DOI: 10.1016/j.athoracsur.2009.10.005]

7 **Vatandoust S**, Price TJ, Karapetis CS. Colorectal cancer: Metastases to a single organ. *World J Gastroenterol* 2015; **21**: 11767-11776 [PMID: 26557001 DOI: 10.3748/wjg.v21.i41.11767]

8 **de Haas RJ**, Wicherts DA, Andreani P, Pascal G, Saliba F, Ichai P, Adam R, Castaing D, Azoulay D. Impact of expanding criteria for resectability of colorectal metastases on short- and long-term outcomes after hepatic resection. *Ann Surg* 2011; **253**: 1069-1079 [PMID: 21451388 DOI: 10.1097/SLA.0b013e318217e898]

9 **Benson AB 3rd**, Venook AP, Cederquist L, Chan E, Chen YJ, Cooper HS, Deming D, Engstrom PF, Enzinger PC, Fichera A, Grem JL, Grothey A, Hochster HS, Hoffe S, Hunt S, Kamel A, Kirilcuk N, Krishnamurthi S, Messersmith WA, Mulcahy MF, Murphy JD, Nurkin S, Saltz L, Sharma S, Shibata D, Skibber JM, Sofocleous CT, Stoffel EM, Stotsky-Himelfarb E, Willett CG, Wu CS, Gregory KM, Freedman-Cass D. Colon Cancer, Version 1.2017, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw* 2017; **15**: 370-398 [PMID: 28275037 DOI: 10.6004/jnccn.2017.0036]

10 **Benoist S**, Pautrat K, Mitry E, Rougier P, Penna C, Nordlinger B. Treatment strategy for patients with colorectal cancer and synchronous irresectable liver metastases. *Br J Surg* 2005; **92**: 1155-1160 [PMID: 16035135 DOI: 10.1002/bjs.5060]

11 **Galizia G**, Lieto E, Orditura M, Castellano P, Imperatore V, Pinto M, Zamboli A. First-line chemotherapy vs bowel tumor resection plus chemotherapy for patients with unresectable synchronous colorectal hepatic metastases. *Arch Surg* 2008; **143**: 352-8; discussion 358 [PMID: 18427022 DOI: 10.1001/archsurg.143.4.352]

12 **Seo GJ**, Park JW, Yoo SB, Kim SY, Choi HS, Chang HJ, Shin A, Jeong SY, Kim DY, Oh JH. Intestinal complications after palliative treatment for asymptomatic patients with unresectable stage IV colorectal cancer. *J Surg Oncol* 2010; **102**: 94-99 [PMID: 20578086 DOI: 10.1002/jso.21577]

13 **Faron M**, Pignon JP, Malka D, Bourredjem A, Douillard JY, Adenis A, Elias D, Bouché O, Ducreux M. Is primary tumour resection associated with survival improvement in patients with colorectal cancer and unresectable synchronous metastases? A pooled analysis of individual data from four randomised trials. *Eur J Cancer* 2015; **51**: 166-176 [PMID: 25465185 DOI: 10.1016/j.ejca.2014.10.023]

14 **Tarantino I**, Warschkow R, Worni M, Cerny T, Ulrich A, Schmied BM, Güller U. Prognostic Relevance of Palliative Primary Tumor Removal in 37,793 Metastatic Colorectal Cancer Patients: A Population-Based,

Propensity Score-Adjusted Trend Analysis. *Ann Surg* 2015; **262**: 112-120 [PMID: 25373464 DOI: 10.1097/SLA.0000000000000860]

15 **Anwar S**, Peter MB, Dent J, Scott NA. Palliative excisional surgery for primary colorectal cancer in patients with incurable metastatic disease. Is there a survival benefit? A systematic review. *Colorectal Dis* 2012; **14**: 920-930 [PMID: 21899714 DOI: 10.1111/j.1463-1318.2011.02817.x]

16 **Li C**, Zheng H, Jia H, Huang D, Gu W, Cai S, Zhu J. Prognosis of three histological subtypes of colorectal adenocarcinoma: A retrospective analysis of 8005 Chinese patients. *Cancer Med* 2019; **8**: 3411-3419 [PMID: 31074597 DOI: 10.1002/cam4.2234]

17 **Li Y**, Feng Y, Dai W, Li Q, Cai S, Peng J. Prognostic Effect of Tumor Sidedness in Colorectal Cancer: A SEER-Based Analysis. *Clin Colorectal Cancer* 2019; **18**: e104-e116 [PMID: 30448100 DOI: 10.1016/j.clcc.2018.10.005]

18 **Tamas K**, Walenkamp AM, de Vries EG, van Vugt MA, Beets-Tan RG, van Etten B, de Groot DJ, Hospers GA. Rectal and colon cancer: Not just a different anatomic site. *Cancer Treat Rev* 2015; **41**: 671-679 [PMID: 26145760 DOI: 10.1016/j.ctrv.2015.06.007]

19 **Biasco G**, Derenzini E, Grazi G, Ercolani G, Ravaioli M, Pantaleo MA, Brandi G. Treatment of hepatic metastases from colorectal cancer: many doubts, some certainties. *Cancer Treat Rev* 2006; **32**: 214-228 [PMID: 16546323 DOI: 10.1016/j.ctrv.2005.12.011]

20 **Mitry E**, Guiu B, Cosconea S, Jooste V, Faivre J, Bouvier AM. Epidemiology, management and prognosis of colorectal cancer with lung metastases: a 30-year population-based study. *Gut* 2010; **59**: 1383-1388 [PMID: 20732912 DOI: 10.1136/gut.2010.211557]

21 **Khattak MA**, Martin HL, Beeke C, Price T, Carruthers S, Kim S, Padbury R, Karapetis CS. Survival differences in patients with metastatic colorectal cancer and with single site metastatic disease at initial presentation: results from South Australian clinical registry for advanced colorectal cancer. *Clin Colorectal Cancer* 2012; **11**: 247-254 [PMID: 22763194 DOI: 10.1016/j.clcc.2012.06.004]

22 **Damiens K**, Ayoub JP, Lemieux B, Aubin F, Saliba W, Campeau MP, Tehfe M. Clinical features and course of brain metastases in colorectal cancer: an experience from a single institution. *Curr Oncol* 2012; **19**: 254-258 [PMID: 23144573 DOI: 10.3747/co.19.1048]

23 **Farnell GF**, Buckner JC, Cascino TL, O'Connell MJ, Schomberg PJ, Suman V. Brain metastases from colorectal carcinoma. The long term survivors. *Cancer* 1996; **78**: 711-716 [PMID: 8756361 DOI: 10.1002/(SICI)1097-0142(19960815)78:4<711::AID-CNCR3>3.0.CO;2-H]

24 **Kruser TJ**, Chao ST, Elson P, Barnett GH, Vogelbaum MA, Angelov L, Weil RJ, Pelley R, Suh JH. Multidisciplinary management of colorectal brain metastases: a retrospective study. *Cancer* 2008; **113**: 158-165 [PMID: 18459179 DOI: 10.1002/cncr.23531]

25 **Amichetti M**, Lay G, Dessì M, Orrù S, Farigu R, Orrù P, Farci D, Melis S; Cagliari Neuro-Oncology Group. Results of whole brain radiation therapy in patients with brain metastases from colorectal carcinoma. *Tumori* 2005; **91**: 163-167 [PMID: 15948545]

26 **Schoeggl A**, Kitz K, Reddy M, Zauner C. Stereotactic radiosurgery for brain metastases from colorectal cancer. *Int J Colorectal Dis* 2002; **17**: 150-155 [PMID: 12049308 DOI: 10.1007/s00384-001-0362-7]

27 **Nozue M**, Oshiro Y, Kurata M, Seino K, Koike N, Kawamoto T, Taniguchi H, Todoroki T, Fukao K. Treatment and prognosis in colorectal cancer patients with bone metastasis. *Oncol Rep* 2002; **9**: 109-112 [PMID: 11748466]

28 **Santini D**, Tampellini M, Vincenzi B, Ibrahim T, Ortega C, Virzi V, Silvestris N, Berardi R, Masini C, Calipari N, Ottaviani D, Catalano V, Badalamenti G, Giannicola R, Fabbri F, Venditti O, Fratto ME, Mazzara C, Latiano TP, Bertolini F, Petrelli F, Ottone A, Caroti C, Salvatore L, Falcone A, Giordani P, Addeo R, Aglietta M, Cascinu S, Barni S, Maiello E, Tonini G. Natural history of bone metastasis in colorectal cancer: final results of a large Italian bone metastases study. *Ann Oncol* 2012; **23**: 2072-2077 [PMID: 22219016 DOI: 10.1093/annonc/mdr572]

29 **Giacchetti S**, Itzhaki M, Gruia G, Adam R, Zidani R, Kunstlinger F, Brienza S, Alafaci E, Bertheault-Cvitkovic F, Jasmin C, Reynes M, Bismuth H, Misset JL, Lévi F. Long-term survival of patients with unresectable colorectal cancer liver metastases following infusional chemotherapy with 5-fluorouracil, leucovorin, oxaliplatin and surgery. *Ann Oncol* 1999; **10**: 663-669 [PMID: 10442188 DOI: 10.1023/a:1008347829017]

30 **Li WH**, Peng JJ, Xiang JQ, Chen W, Cai SJ, Zhang W. Oncological outcome of unresectable lung metastases without extrapulmonary metastases in colorectal cancer. *World J Gastroenterol* 2010; **16**: 3318-3324 [PMID: 20614489 DOI: 10.3748/wjg.v16.i26.3318]

31 **Manfredi S**, Lepage C, Hatem C, Coatmeur O, Faivre J, Bouvier AM. Epidemiology and management of liver metastases from colorectal cancer. *Ann Surg* 2006; **244**: 254-259 [PMID: 16858188 DOI: 10.1097/01.sla.0000217629.94941.cf]

32 **D'Agostino RB Jr**. Propensity score methods for bias reduction in the comparison of a treatment to a non-randomized control group. *Stat Med* 1998; **17**: 2265-2281 [PMID: 9802183 DOI: 10.1002/(sici)1097-0258(19981015)17:19<2265::aid-sim918>3.0.co;2-b]

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