Research Article

Female Colon Cancer Metastasis Pattern and Prognosis: A SEER-Based Study

Yurong Liu, Rongbin Kang, Huida Zheng, Pengcheng Wang, Weixin Jiang, Bin Xiong, Jintao Chen, and Jianhua Xu

1Department of Gastrointestinal Surgery, The Second Affiliated Hospital of Fujian Medical University, Quanzhou, China
2Department of Gastric Surgery, Fujian Medical University Union Hospital, Fuzhou, China
3Department of Endocrinology, The Affiliated Hospital of Qingdao University, Qingdao, China

Correspondence should be addressed to Jianhua Xu; xjh630913@126.com

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The purpose of this study was to compare the metastatic pattern and prognosis of female colon cancer (FCC) to that of male colon cancer (MCC) to ascertain the independent factors impacting the prognosis of patients with FCC. The data of the present study population were retrieved from the Surveillance, Epidemiology, and End Results (SEER) database. Descriptive analysis, the Kaplan-Meier method, and the Cox regression were used to evaluated FCC characteristics and factors associated with prognosis. There were 56,442 patients diagnosed with FCC, of whom 8,817 had distant metastases. Compared to patients with nonmetastatic FCC, a greater proportion of metastatic FCC patients was less than 60 years of age, black race, and grade III-IV. The primary sites were mainly located on the left side and have more possibility to receive chemotherapy and radiotherapy. Compared to metastatic MCC, a higher proportion of metastatic FCC patients ranged over 60 years of age, black race, treated without chemotherapy, and insurance, while the primary site was located on the right side. Liver and lung were the two most common sites of solitary metastases in CC, and among patients with solitary metastases in CC, patients who had lung metastases had a better prognosis than those who developed other types of metastasizes. Patients with FCC with metastases of the liver had a worse prognosis than their MCC counterparts. Cox multivariate regression analysis showed that the risk ratio was higher in metastatic FCC patients compared to those without metastases. We report the survival comparison of metastatic FCC with nonmetastatic FCC through the SEER database. Our results suggest that it has unique clinicopathological features and differs from metastatic MCC. Furthermore, patients with liver metastatic FCC have a worse prognosis than those with MCC. Emphasis on screening for colon cancer in women and additional clinical care should be paid for, especially for patients with FCC with metastatic liver cancer.

1. Introduction

Colon cancer (CC) is the third most prevalent cancer in the United States, occurring in both men and women, and is also the third leading cause of mortality from cancer [1]. The cumulative risk of developing colon cancer before 75 years is 1.51% and 1.12% for men and women, respectively, giving a rate of 1 in 66 men and 1 in 89 women to develop CC [2]. Despite recent advances in chemotherapy and radiotherapy for CC, surgical resection remains the primary treatment, but there are gender differences in CC treatment choices [3, 4].

In general, gender may be the first patient characteristic to be considered when discussing tumor differences between patient subgroups. Gender differences in tumor behavior exist in patients with colon cancer [5], but the exact mechanisms are unknown. The high mortality rate of colon cancer is mainly due to distant metastases, and the degree of CC differentiation and histopathological type is all factors that affect the prognosis of CC patients [6, 7], while the clinical characteristics, metastatic patterns, and factors related to the prognosis in FCC with distant metastases have not been thoroughly described, which means these variables in the patient populations remain in uncharted territory for this
type of disease to be explored. Thus, we identified the FCC data recorded in this study from 2010 to 2015 in the SEER database. We conducted cross-sectional and longitudinal studies of patients with metastatic FCC to determine their clinicopathological characteristics and differences from patients with metastatic MCC and identify independent factors that affect the prognosis of patients with FCC.

2. Method

2.1. Populations and Characteristics. The data for this study were extracted from the National Cancer Institute's SEER-18 database, using the National Cancer Institute's SEER*Stat version 8.3.9 (http://http://www.SEER.cancer.gov/seerstat). Patients included in the study were those ≥18 years old histologically diagnosed with colon cancer between 2010 and 2015. The inclusion criteria were as follows: (a) ICD-O-3 site codes: cecum, ascending colon, hepatic flexure of colon, transverse colon, splenic flexure of colon, descending colon, and sigmoid colon; overlapping lesion of colon and colon NOS; (b) colon cancer was the only primary malignancy; and (c) patients who were under active follow-up; furthermore, patients who met the following criteria were excluded: (a) patients with additional primary cancers, (b) patients with no information on the status of distant organ metastases, (c) unknown autopsy or death certificate diagnoses and diagnoses not confirmed by pathology, and (d) unknown survival months. After completing the necessary screening, we were able to identify 114039 individuals who were qualified for survival analysis and other investigations (Figure 1).

The patients were separated into two groups: FCC and MCC. The AJCC 7th edition was used to determine clinicopathological staging [8]. Age, race, primary site, histology, pathological grade, AJCC TNM stage, surgery, radiotherapy and chemotherapy information, marital status, and insurance status were included as research parameters.

2.2. Statistical Analysis. To summarize demographic and clinical factors, we performed descriptive statistics. The Pearson chi-square test and Fisher exact probability method were utilized to evaluate clinicopathological variables between cohorts. The overall survival (OS) of patients with MCC and FCC with distinct metastatic organs was analyzed by Kaplan-Meier and log-rank test. In addition, we looked for other factors that could impact prognosis using univariate and multivariate Cox proportional risk models. All the tests were two-sided, and statistical significance was defined as $P < 0.05$. The SEER*Stat program version 8.3.9 was used to collect all of the data. All statistical analyses were conducted using R software version 4.0.4.

3. Results

3.1. Patient Clinicopathological Data. A total number of 56442 FCC patients were enrolled in the study. 8817 cases (15.6%) of these FCC patients had distant metastases. A higher proportion of FCC patients with distant metastases were younger than 60 years, black, grades III-IV receiving chemotherapy and radiotherapy, and married than FCC patients without metastases. The proportion of patients with the primary site in the right colon, surgery, and insurance was lower. Table 1 shows the detailed patient clinical characteristics. Patients with FCC with distant organ metastases had more diagnoses than MCC age > 60 years, black race, right colon, unmarried, and with insurance; the former were less likely to receive chemotherapy than the latter. Both groups had identical pathology, pathological grading, TN stage, surgery, and radiation.

FCC: female colon cancer; MCC: male colon cancer. ^Comparison between male colon cancer without metastasis and male colon cancer with metastasis. *Comparison between male colon cancer with metastasis and female colon cancer with metastasis. **Comparison between female colon
Table 1: Clinical characteristics of male and female patients with colon cancer.

|                      | MCC without metastasis | MCC with metastasis | FCC without metastasis | FCC with metastasis | P value^ | P value* | P value^# |
|----------------------|------------------------|---------------------|------------------------|---------------------|-----------|----------|-----------|
|                      | N = 47277 % 82.1       | N = 10320 % 17.9    | N = 47625 % 84.4       | N = 8817 % 15.6     |           |          |           |
| Age at diagnosis (year) |                       |                     |                        |                     | .000**    | .000***  | .000**    |
| ≤60                  | 17668 37.4             | 4430 42.9           | 14952 31.4             | 3546 40.2           |           |          |           |
| >60                  | 29609 62.6             | 5890 57.1           | 32673 68.6             | 5271 59.8           |           |          |           |
| Race                 |                        |                     |                        |                     | .000**    | .000**   | .000**    |
| Black                | 5541 11.7              | 1652 16.0           | 6292 13.2              | 1617 18.3           |           |          |           |
| White                | 36598 77.4             | 7727 74.9           | 36343 76.3             | 6362 72.2           |           |          |           |
| Others               | 4570 9.67              | 919 8.91            | 4522 9.50              | 822 9.32            |           |          |           |
| Unknown              | 568 1.20               | 22 0.21             | 468 0.98               | 16 0.18             |           |          |           |
| Primary site         |                        |                     |                        |                     | .000**    | .000**   | .000**    |
| Right colon          | 22445 47.5             | 4243 41.1           | 26482 55.6             | 4183 47.4           |           |          |           |
| Left colon           | 23686 50.1             | 5264 51.0           | 20023 42.0             | 3812 43.2           |           |          |           |
| Overlapping lesion   | 532 1.13               | 138 1.34            | 570 1.20               | 132 1.50            |           |          |           |
| Unknown              | 614 1.30               | 675 6.54            | 550 1.15               | 690 7.83            |           |          |           |
| Histopathology type  |                        |                     |                        |                     | .000**    | 0.912    | .000**    |
| Adenocarcinoma       | 45618 96.5             | 9742 94.4           | 45729 96.0             | 8319 94.4           |           |          |           |
| Others               | 1659 3.51              | 578 5.60            | 1896 3.98              | 498 5.65            |           |          |           |
| Pathology grade      |                        |                     |                        |                     | .000**    | 0.063    | .000**    |
| (I) Well-differentiated | 4399 9.30             | 382 3.70            | 4197 8.81              | 333 3.78            |           |          |           |
| (II) Moderately      | 30045 63.6             | 5326 51.6           | 29583 62.1             | 4390 49.8           |           |          |           |
| (III) Poorly differentiated | 5895 12.5         | 1841 17.8           | 7334 15.4              | 1577 17.9           |           |          |           |
| (IV) Undifferentiated | 1244 2.63             | 348 3.37            | 1615 3.39              | 337 3.82            |           |          |           |
| Unknown              | 5694 12.0              | 2423 23.5           | 4896 10.3              | 2180 24.7           |           |          |           |
| T                    |                        |                     |                        |                     | 0.000     | 0.697    | 0.000     |
| T0-T2                | 18260 38.6             | 1276 33.9           | 17413 36.6             | 1055 12.0           |           |          |           |
| T3-T4                | 27645 58.5             | 6175 59.8           | 28741 60.3             | 5293 60.0           |           |          |           |
| Unknown              | 1372 2.9               | 2869 27.8           | 1471 3.1               | 2469 28.0           |           |          |           |
| N                    |                        |                     |                        |                     | 0.000     | 0.117    | 0.000     |
| N0                   | 30765 65.1             | 3199 31.0           | 30468 64.0             | 2786 31.6           |           |          |           |
| N1                   | 10342 21.9             | 3382 32.8           | 10681 22.4             | 2746 31.1           |           |          |           |
| N2                   | 5501 11.6              | 2520 24.4           | 5788 12.2              | 2222 25.2           |           |          |           |
| Unknown              | 699 1.4                | 1219 11.8           | 688 1.4                | 1063 12.1           |           |          |           |
| Surgery              |                        |                     |                        |                     | .000**    | 0.356    | .000**    |
| No                   | 2635 5.57              | 4653 45.1           | 2625 5.51              | 3958 44.9           |           |          |           |
| Yes                  | 44578 94.3             | 5647 54.7           | 44939 94.4             | 4849 55.0           |           |          |           |
| Unknown              | 64 0.14                | 20 0.19             | 61 0.13                | 10 0.11             |           |          |           |
| Radiotherapy         |                        |                     |                        |                     | .000**    | 0.145    | .000**    |
| No                   | 45314 95.8             | 9715 94.1           | 46271 97.2             | 8344 94.6           |           |          |           |
| Yes                  | 1963 4.15              | 605 5.86            | 1354 2.84              | 473 5.36            |           |          |           |
| Chemotherapy         |                        |                     |                        |                     | .000**    | .000**   | .000**    |
| No                   | 33412 70.7             | 3473 33.7           | 34496 72.4             | 3227 36.6           |           |          |           |
| Yes                  | 13865 29.3             | 6847 66.3           | 13129 27.6             | 5590 63.4           |           |          |           |
| Marital status       |                        |                     |                        |                     | .000**    | .000**   | .000**    |
| Married              | 28733 60.8             | 5875 56.9           | 20114 42.2             | 3757 42.6           |           |          |           |
| Unmarried            | 15497 32.8             | 3931 38.1           | 24252 50.9             | 4600 52.2           |           |          |           |
| Unknown              | 3047 6.44              | 514 4.98            | 3259 6.84              | 460 5.22            |           |          |           |
cancer without metastasis and female colon cancer with metastasis. ∗P < 0.05, ∗∗P < 0.001.

3.2. Metastasis Pattern. The majority (76.56%) of the cohort of FCC with distant metastasis had single site distant metastases. The most common location of metastases was the liver, which represented 68.49% of the patients. The number of lung metastasis accounted for 593 (6.73%). Very few patients had bone or brain metastasis. Concerning the differences in metastasis patterns between FCC and MCC, MCC patients had a lower proportion of brain metastases only than their FCC counterparts (0.33% vs 0.53%), as well as lung metastases only (5.5% vs 6.73%), whereas the percentage of bone and liver metastases was higher in MCC patients (Table 2).

### Table 1: Comparison of organ metastasis patterns between male and female patients with colon cancer.

| Variable                        | Male (n = 10320) | Female (n = 8817) | P value |
|---------------------------------|------------------|-------------------|---------|
| Bone metastasis only            | 100              | 71                | 0.230   |
| Brain metastasis only           | 34               | 4                 | 0.031   |
| Liver metastasis only           | 7107             | 6039              | 0.579   |
| Lung metastasis only            | 568              | 593               | <.001   |
| Bone and brain                  | 4                | 4                 | 0.824   |
| Bone and liver                  | 275              | 196               | 0.049   |
| Bone and lung                   | 52               | 40                | 0.617   |
| Brain and liver                 | 29               | 23                | 0.790   |
| Liver and lung                  | 1826             | 1564              | 0.936   |
| Bone, brain, and liver          | 11               | 8                 | 0.729   |
| Bone, brain, and lung           | 6                | 4                 | 0.700   |
| Bone, liver, and lung           | 222              | 165               | 0.171   |
| Brain, liver, and lung          | 40               | 36                | 0.820   |
| Bone, brain, liver, and lung    | 24               | 10                | 0.051   |
| One site metastasis             | 7809             | 6750              | 0.151   |
| Two site metastasis             | 2208             | 1844              | 0.498   |
| Three site metastasis           | 279              | 213               | 0.210   |
| Four site metastasis            | 24               | 10                | 0.051   |

*

3.3. Survival Analysis. Among patients with metastatic colon cancer by gender, liver metastases only, lung metastases only, and combined liver metastases with lung metastases accounted for more than 90% of the total metastatic population. We included these three groups in our survival and prognosis analyses to investigate the influence of distant metastases on prognosis. Kaplan-Meier analysis showed that for patients with liver metastases only, the survival rate of MCC patients was better than that of FCC patients and was statistically significant (P = 0.0058), while for the other two groups, our analysis showed no statistical difference in OS by gender (Figure 2).

However, it appears that patients between those three groups and nonmetastatic FCC were significantly different (Figure 3).
### Figure 2: OS rate of MCC and FCC patients at different metastasis sites.

(a) OS of liver alone metastasis between MCC and FCC patients. 
(b) OS of lung alone metastasis between MCC and FCC patients. 
(c) OS of both liver and lung metastasis between MCC and FCC patients.

**FCC:** female colon cancer; **MCC:** male colon cancer; **OS:** overall survival.

#### Table: Number at risk for different strata

| Strata          | Male | Female |
|-----------------|------|--------|
| (a) Liver alone | 7107 | 6039   |
| (b) Lung alone  | 568  | 593    |
| (c) Both        | 1826 | 1564   |

**Survival time (Months)**

| Strata          | Male | Female |
|-----------------|------|--------|
| (a) Liver alone | 3533 | 2779   |
| (b) Lung alone  | 291  | 308    |
| (c) Both        | 640  | 552    |

**Percent survival (%)**

| Strata          | Male | Female |
|-----------------|------|--------|
| (a) Liver alone | 1542 | 1190   |
| (b) Lung alone  | 130  | 137    |
| (c) Both        | 47   | 49     |

**Strata**

- **Male**
- **Female**

**Survival time (Months)**

| Strata          | Male | Female |
|-----------------|------|--------|
| (a) Liver alone | 583  | 512    |
| (b) Lung alone  | 54   | 58     |
| (c) Both        | 218  | 239    |

**Number at risk**

| Strata          | Male | Female |
|-----------------|------|--------|
| (a) Liver alone | 239  | 218    |
| (b) Lung alone  | 20   | 23     |
| (c) Both        | 62   | 58     |

**Percent survival (%)**

| Strata          | Male | Female |
|-----------------|------|--------|
| (a) Liver alone | 239  | 218    |
| (b) Lung alone  | 20   | 23     |
| (c) Both        | 62   | 58     |

**Survival time (Months)**

| Strata          | Male | Female |
|-----------------|------|--------|
| (a) Liver alone | 3  | 15     |
| (b) Lung alone  | 1    | 11     |
| (c) Both        | 3   | 47     |

**Percent survival (%)**

| Strata          | Male | Female |
|-----------------|------|--------|
| (a) Liver alone | 1    | 15     |
| (b) Lung alone  | 11   | 47     |
| (c) Both        | 3   | 47     |

**Survival time (Months)**

| Strata          | Male | Female |
|-----------------|------|--------|
| (a) Liver alone | 3   | 15     |
| (b) Lung alone  | 1    | 11     |
| (c) Both        | 3   | 47     |
Survival rates decreased as the number of metastatic sites increased in patients with metastatic FCC (Figure 4). The Cox univariate analysis revealed that age, race, tumor primary site, histopathology type, pathology grade, TN stage, surgery, chemotherapy, marital status, insurance situation, and the metastatic sites were independent factors affecting OS ($P < 0.001$), and these variables were included in the multivariate model (Table 3). In detail, black, age $> 60$ years, primary tumor site in the right colon or the overlapping lesion, nonadenocarcinoma, pathological grade II, grade III, and grade IV, distant metastasis, treatment without surgery and chemotherapy, single, and distant metastasis correlated with poor prognosis. Radiation therapy did not affect the outcome of this study.

4. Discussion

In both men and women, colon cancer is one of the most prevalent causes of cancer development. Despite recent advances in CC screening, diagnosis, and treatment, the long-term prognosis of CC patients remains poor [8]. The prognosis of patients with metastatic and nonmetastatic FCC was compared with patients with MCC. To our knowledge, this study is the first gender-focused metastasis model-based analysis of colon cancer data.

In this study, the metastasis rate was 17.9% versus 15.6% in male versus female colon cancer patients, respectively. The incidence of colon cancer increased significantly with age. According to past research, younger CC patients are more likely to develop metastases than older patients and have limited surgical and chemotherapeutic treatment [9]. Similarly, younger CC patients in this study developed metastases significantly more than older CC patients, and when women were diagnosed with colon cancer, they were significantly older than men and presented with more severe disease. This may be explained by the lower rate of screening colonoscopy in women over 65 years of age than men of the same age [10]. A higher rate of incomplete colonoscopy in women has also been reported [11], contributing to more colon cancers in women of advanced age. The population was more than 3/4 white in the data we included, but we found that black CC patients were more likely to have distant metastases, consistent with previously reported results [12]. Previous studies have demonstrated a lack of awareness of screening guidelines in general and in African American men in particular [13, 14].

Furthermore, black patients with metastatic colorectal cancer are less likely to get chemotherapy or have liver metastasectomy, and they are less likely to discuss or contemplate participating in studies [15, 16]. The primary location of the tumor is strongly associated with patient prognosis, as reported in different types of cancer [17–19]. In the same vein, Ishihara et al. [20] found that proximal indolent cell carcinoma is considered a distinct subgroup with a good tumor prognosis in colon cancer. Our analysis from a gender perspective showed that the primary tumor location of FCC was more often located in the right colon than MCC, which is consistent with previous reports [4]. In patients with colon cancer, researchers developed a nomogram that predicted risk variables for liver and lung

**Figure 3:** The survival difference among the different metastasis sites in FCC patients. FCC: female colon cancer.
metastasis, with tumor site being an independent risk factor for metastasis [21]. As we mentioned earlier, women have a higher rate of incomplete colonoscopy [9]. In addition, some women tend to have a more extended colon cross-section and smaller bowel diameter, making standard colonoscopy equipment usually unsuitable for this group of women [22]. Therefore, we recommend that women need to choose a thinner colonoscopy device for a complete colonoscopy when undergoing colon cancer screening to reduce the number of missed right colon cancer due to the device and physiological configuration.

The preference for chemotherapy and radiation therapy over surgery in advanced cancers may also explain why patients with metastatic FCC rarely undergo surgery. However, treatment of stage IV colon cancer remains challenging, and despite recent advances in chemotherapy and other palliative treatment modalities, the best treatment options for colon cancer with unresectable metastases remain to be elucidated. Interestingly, the number of patients treated with radiation is more than 6% for male and female patients. Adjuvant external beam radiation is usually not recommended due to the difficulty of targeting and the proximity of critical surrounding structures (e.g., small intestine), as these factors can limit the dose that can kill the tumor. Recent findings show that adjuvant radiotherapy can significantly prolong OS in patients with advanced local disease (pT4) and positive cut margins [23]; therefore, adjuvant therapy for CC patients should not be abandoned due to the limitations of RT. Hypodifferentiated versus undifferentiated colon cancer is more likely to develop distant metastases, and there is no difference between men and women.

Although modern research has been able to elucidate the pathogenesis of CC and provide effective screening strategies, the prevalence of CC is still increasing. A better understanding of the occurrence, progression, and metastasis of CC can help develop molecular markers for early detection and risk stratification methods to improve clinical care for CC patients. We compared distant metastasis patterns in patients with MCC and FCC in depth using the SEER database to understand the survival differences between patients with different metastasis patterns. Single-site metastases occurred in more than three-quarters of the total number of patients. Overall, the liver and brain were the most common and least common sites of solitary metastases in patients with CC, respectively, consistent with prior reports [24]. Due to the blood-brain barrier, fewer patients had brain metastases alone (0.33% vs. 0.53%), but when combined with metastases from other sites, brain metastases exceeded 1% in both sexes.

Similarly, when lung metastases were combined with liver metastases, the number of patients was much higher than that of patients with lung metastases alone. We believe that once a tumor develops distant metastasis in one organ, it may accelerate metastasis in other sites; although, brain metastasis alone is uncommon when it has metastasis in other sites. Interestingly, FCC was more likely to have a
Table 3: Univariate and multivariate survival analysis of female colon cancer patients with liver alone, lung alone, and simultaneous liver and lung metastasis.

| Characteristics          | Univariate analysis | Hazard ratio | 95% CI     | Multivariate analysis | P value |
|--------------------------|---------------------|--------------|------------|-----------------------|---------|
|                          | P value             |              |            |                       |         |
| Age at diagnosis (year)  | <.001               |              |            |                       | <.001   |
| ≤60                      | Reference            |              |            |                       |         |
| >60                      | 1.78                | 1.72-1.84    | <.001      |                       |         |
| Race                     | <.001               |              |            |                       | <.001   |
| Black                    | Reference            |              |            |                       |         |
| White                    | 0.98                | 0.95-1.02    | 0.4443     |                       |         |
| Others                   | 0.84                | 0.79-0.90    | <.001      |                       |         |
| Unknown                  | 0.11                | 0.07-0.19    | <.001      |                       |         |
| Primary site             | <.001               |              |            |                       | <.001   |
| Right colon              | Reference            |              |            |                       |         |
| Left colon               | 0.87                | 0.84-0.90    | <.001      |                       |         |
| Overlapping lesion       | 1.15                | 1.03-1.28    | 0.0154     |                       |         |
| Unknown                  | 1.27                | 1.18-1.39    | <.001      |                       |         |
| Histopathology type      | <.001               |              |            |                       | <.001   |
| Adenocarcinoma           | Reference            |              |            |                       |         |
| Others                   | 1.17                | 1.1-1.24     | <.001      |                       |         |
| Pathology grade          | <.001               |              |            |                       | <.001   |
| (I) Well-differentiated  | Reference            |              |            |                       |         |
| (II) Moderately          | 1.15                | 1.08-1.23    | <.001      |                       |         |
| (III) Poorly differentiated | 1.62           | 1.51-1.74    | <.001      |                       |         |
| (IV) Undifferentiated    | 1.94                | 1.77-2.11    | <.001      |                       |         |
| Unknown                  | 1.17                | 1.09-1.26    | <.001      |                       |         |
| T stage                  | <.001               |              |            |                       | <.001   |
| T0-T2                    | Reference            |              |            |                       |         |
| T3-T4                    | 1.93                | 1.85-2.01    | <.001      |                       |         |
| Unknown                  | 1.53                | 1.44-1.63    | <.001      |                       |         |
| N stage                  | <.001               |              |            |                       |         |
| N0                       | Reference            |              |            |                       |         |
| N1                       | 1.70                | 1.63-1.76    | <.001      |                       |         |
| N2                       | 3.22                | 3.09-3.37    | <.001      |                       |         |
| Unknown                  | 1.32                | 1.23-1.41    | <.001      |                       |         |
| Surgery                  | <.001               |              |            |                       | <.001   |
| No                       | Reference            |              |            |                       |         |
| Yes                      | 0.17                | 0.16-0.18    | <.001      |                       |         |
| Unknown                  | 0.53                | 0.38-0.76    | <.001      |                       |         |
| Radiotherapy             | 0.277               |              |            |                       |         |
| No                       | Reference            |              |            |                       |         |
| Yes                      | Chemotherapy         | <.001        |            | <.001                 |         |
| No                       | Reference            |              |            |                       |         |
| Yes                      | 0.47                | 0.45-0.48    | <.001      |                       |         |
| Marital status           | <.001               |              |            |                       | <.001   |
| Married                  | Reference            |              |            |                       |         |
| Unmarried                | 1.41                | 1.37-1.45    | <.001      |                       |         |
| Unknown                  | 1.12                | 1.05-1.19    | 0.0312     |                       |         |
| Insurance situation      | <.001               |              |            |                       | <.001   |
single lung metastasis than MCC; yet, we found no significant difference in their OS.

The clinicopathological characteristics and metastatic patterns of metastatic MCC and FCC were different in the present study. Multivariate Cox regression showed that in patients with FCC, advanced age, primary site in the right colon, higher pathological grade, and distant organ metastasis were independent risk factors affecting the prognosis of patients with FCC (Table 3). The most common site of distant metastasis in patients with CC is the liver, but we found differences in prognosis by gender, and the survival of patients with single liver metastasis in FCC was significantly lower than that of MCC in the same group ($P=0.0058$). Once the tumor metastasized, patient survival decreased, the OS decreased more with increasing metastatic sites, and the same results have been reported in other tumors [24, 25]. Liver and lung are the two most common sites of solitary metastases in FCC [26], but there are differences in OS in patients with these two metastases. The OS of patients with solitary lung metastasis was significantly higher than that of patients with solitary liver metastasis. Reasons for the difference still need further exploration. However, there are some limitations which worth further more research; firstly, the BMI and BSA of patients were not included in this study, and the prospective study already completed by Thygesen et al. [27] demonstrated that obesity and overweight are key variable risk factors for colon cancer. With this finding, they advocate public health interventions to avoid risks due to weight gain as a way to better prevent colon cancer. Secondly, the data source used in this study was the SEER database. We were only able to study this with the available information on four organ metastases, namely, liver, lung, bone, and brain, due to the inability to obtain data on other metastasis sites, and we cannot conduct a more comprehensive study. Finally, there are differences in metastatic patterns between males and females, but we could not determine which factors are associated with them. That said, further research to clarify the rationale underlying these differences is necessary.

5. Conclusion

Our population-based analysis of 114,039 CC patients found that older women were diagnosed with colon cancer, and that advanced age at diagnosis (>60 years) significantly predicted worsening OS. The primary site of FCC was more likely to be in the right colon. Female patients may be more likely to have pulmonary metastases; although the most common distant sites of metastasis for both FCC and MCC are liver and lung, patients with liver metastases from FCC have a worse prognosis than their MCC counterparts, and we also found that patients with liver metastases from FCC have a worse prognosis than those with pulmonary metastases. The results of this study have some reference value for clinicians in dealing with CC patients, who should pay attention to colon cancer screening in women and should actively receive treatment for FCC patients with liver metastases and lung metastases to improve their prognosis.

### Data Availability

The data supporting this study’s results are available from the corresponding author on request.

### Disclosure

A preprint has previously been published [28].

### Conflicts of Interest

The authors declare that they have no competing interests.

### Authors’ Contributions

Liu YR, Kang RB, Zheng HD, and Xu JH designed the study. Wang PC, Jiang WX, and Xiong B contributed to the literature search. Liu YR, Jiang WX, and Chen JT extracted and analyzed the data. Liu YR and Kang RB wrote the paper. Liu YR and Kang RB contributed equally to this work and should be considered as co-first authors. All authors contributed to the article and approved the submitted version. Yurong Liu and Rongbin Kang contributed equally to this work.

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References

[1] R. L. Siegel, K. D. Miller, and A. Jemal, “Cancer statistics, 2020,” CA: a Cancer Journal for Clinicians, vol. 70, no. 1, pp. 7–30, 2020.

[2] F. Bray, J. Ferlay, I. Soerjomataram, R. L. Siegel, L. A. Torre, and A. Jemal, “Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries,” CA: a Cancer Journal for Clinicians, vol. 68, no. 6, pp. 394–424, 2018.

[3] J. S. Oliver, M. Y. Martin, L. Richardson, Y. Kim, and M. Pisu, “Factors associated with colorectal cancer screening among younger African American men: a systematic review,” Annals of Surgical Oncology, vol. 27, no. 3, pp. 825–832, 2020.

[4] J. Wang, S. Li, Y. Liu, C. Zhang, H. Li, and B. Lai, “Metastatic patterns and survival outcomes in patients with stage IV colon cancer: a population-based analysis,” Cancer Medicine, vol. 9, no. 1, pp. 361–373, 2020.

[5] R. Wang, Y. Zhu, X. Liu, X. Liao, J. He, and L. Niu, “The Clinicopathological features and survival outcomes of patients with different metastatic sites in stage IV breast cancer,” BMC Cancer, vol. 19, no. 1, p. 1091, 2019.

[6] M. Riihimäki, A. Hemminki, M. Fallah et al., “Predictive nomograms for synchronous liver and lung metastasis in colon cancer,” Journal of Gastrointestinal Cancer, vol. 51, no. 3, pp. 925–931, 2020.

[7] A. Gaitanidis, N. Machairas, M. Alevizakos, C. Tsalikidis, A. Tsaroucha, and M. Pittakoudis, “Predictive nomograms for synchronous liver and lung metastasis in colon cancer,” Journal of Gastrointestinal Cancer, vol. 51, no. 3, pp. 925–931, 2020.

[8] S. Ishihara, T. Watanabe, T. Akahane et al., “Tumor location is a prognostic factor in poorly differentiated adenocarcinoma, mucinous adenocarcinoma, and signet-ring cell carcinoma of the colon,” International Journal of Colorectal Disease, vol. 27, no. 3, pp. 371–379, 2012.

[9] J. G. Mygatt, J. Cullen, S. A. Streicher et al., “Race, tumor location, and disease progression among low-risk prostate cancer patients,” Cancer Medicine, vol. 9, no. 6, pp. 2235–2242, 2020.

[10] Q. Shan, Z. Li, J. Lin et al., “Tumor primary location may affect metastasis pattern for patients with stage IV NSCLC: a population-based study,” Journal of Oncology, vol. 2020, 2020.

[11] J. N. Bliton, M. Parides, P. Muscarella, K. T. Papalezova, and H. In, “Understanding racial disparities in gastrointestinal cancer outcomes: lack of surgery contributes to lower survival in African American patients,” Cancer Epidemiology, Biomarkers & Prevention, vol. 30, no. 3, pp. 529–538, 2021.

[12] F. Bray, J. Ferlay, I. Soerjomataram, R. L. Siegel, L. A. Torre, and A. Jemal, “Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries,” CA: a Cancer Journal for Clinicians, vol. 68, no. 6, pp. 394–424, 2018.