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Original Article

Comparison of 627 patients with right- and left-sided colon cancer in China: Differences in clinicopathology, recurrence, and survival

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Abstract

Objective: Recent studies have reported increased mortality for right-sided colon cancers; however, the results are conflicting for different stage tumors. We examined the differences in clinicopathology between right- and left-sided colon cancers and the relationships between colon cancer location (right- and left-side) and 5-year disease-free survival (DFS) and overall survival (OS).

Methods: We identified patients from 2005 to 2008 with stage II/III colon cancer who underwent surgery for curative intent. We explored the impact of the tumor location on the postoperative DFS and OS using univariate and multivariate analyses.

Results: Of 627 patients, 50.6% (317/627) had right-sided colon cancer. These patients were more likely to have weight loss, second primary tumor, elevated preoperative carbohydrate antigen 19-9 (CA19-9), increased incidence of non-adenocarcinoma, more poorly differentiated tumors, vascular invasion, defective mismatch repair, and a lighter smoking history ($P < 0.05$). Right-sided colon cancer had a higher recurrence incidence compared with left-sided cancer (30.6% *vs.* 23.2%, $P = 0.037$), particularly with multiple metastatic sites in the first recurrence (17.5% *vs.* 5.6%, $P = 0.020$). Kaplan−Meier survival curves demonstrated a significant difference in the 5-year DFS rate between right- and left-sided cancers across all stages (68.1% *vs.* 75.2%, $P = 0.043$). However, there was no significant difference in the 5-year OS rate between the two groups (73.8% *vs.* 79.0%, $P = 0.103$). Subgroup analysis demonstrated that patients with left-sided colon cancer had a significantly better 5-year DFS and OS rates compared with those with right-sided disease at stage III (64.3% *vs.* 46.8%, $P = 0.002$; 69.5% *vs.* 53.5%, $P = 0.006$, respectively); there were no significant differences in the 5-year DFS and OS rates at stage II (85.2% *vs.* 85.9%, $P = 0.819$; 89.8% *vs.* 88.5%, $P = 0.803$, respectively). Adjusted Cox regression analysis showed no significant differences in the 5-year OS and DFS rates for stage II [hazard ratio (*HR*) = 1.203, 95% confidence interval (*CI*): 0.605−2.391, $P = 0.598$; *HR* = 0.980, 95%

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CI: 0.542–1.774, $P = 0.948$, respectively] or all stages combined (*HR* = 0.867, 95% *CI*: 0.613–1.227, $P = 0.421$; *HR* = 0.832, 95% *CI*: 0.606–1.142, $P = 0.255$, respectively). However, stage III left-sided cancer had higher 5-year OS and DFS rates (*HR* = 0.626, 95% *CI*: 0.414–0.948, $P = 0.027$; *HR* = 0.630, 95% *CI*: 0.428–0.926, $P = 0.019$, respectively).

Conclusion: We found that right- and left-sided colon cancers had significantly different clinicopathological characteristics. Right-sided colon cancer had a higher incidence of recurrence than left-sided disease. Patients with stage III right-sided colon cancer had a worse prognosis compared with those with stage III left-sided colon cancer.

Keywords: Colon cancer; Location; Recurrence; Survival

Introduction

Colorectal cancer (CRC) is the third most commonly diagnosed cancer in men and the second in women, with an estimated 1.4 million cases and 693,900 deaths occurring in 2012 worldwide.[1] In China, the incidence of CRC is increasing rapidly and it is now ranked fifth in terms of morbidity and mortality among all malignancies.[2] Studies have shown that right-sided colon cancers are becoming more prevalent, with a decline in the incidence of left-sided colon cancers.[3,4] It has been suggested that there may be two distinct categories of cancer: right- and left-sided colon cancers that arise proximally and distally to the splenic flexure, respectively.[5] Subsequently, several studies have proposed explanations for this difference including genetic, environmental, and embryological factors.[5–7] The primary tumor location has prognostic importance that is related to targeted therapy response in patients with metastatic CRC.[8,9] In 13 first-line randomized controlled trials and one prospective pharmacogenetic study, right-sided colon cancer is associated with a significantly worse prognosis compared to left-sided colon cancer [hazard ratio (*HR*) for overall survival (OS) = 1.56, 95% confidence interval (*CI*): 1.43–1.70, $P < 0.001$)].[8] A meta-analysis of FIRE-3/AIO KRK0306, CALGB/SWOG 80405, and PEAK studies indicated that patients with *RAS* wild-type left-sided colon cancer had a significantly greater survival benefit from the addition of anti-epidermal growth factor receptor (EGFR) treatment compared with anti-vascular endothelial growth factor (VEGF) treatment to standard chemotherapy (*HR* = 0.71, 95% *CI*: 0.58–0.85, $P = 0.0003$).[8]

However, there has been conflicting information regarding the relationship between cancer location and prognosis in patients with stage I–III disease.[10–17] Some studies indicated that right-sided colon cancer has been associated with worse survival than left-sided colon cancer.[10,12] A meta-analysis of 66 studies ($n = 1{,}437{,}846$ patients) with a median follow-up of 65 months revealed that left-sided primary tumor location was associated with a significantly reduced risk of death (*HR* = 0.82, 95% *CI*: 0.79–0.84, $P < 0.001$) independent of the stage.[16] Weiss et al[13] reported no overall difference in 5-year mortality between right- and left-sided colon cancers but found that within stage II disease right-sided cancers had lower mortality while within stage III right-sided cancers had higher mortality. However, Moritani et al[14] found that patients with stage I right-sided colon cancer had a significantly higher 5-year disease-free survival (DFS) rate than did those with left-sided disease; however, there was no significant difference at stages II and III. A population-based analysis of stage I–III colon cancer provided evidence that in stages I and II, the prognosis of right-sided cancer was better for OS (*HR* = 0.89; 95% *CI*: 0.84–0.94 and *HR* = 0.85, 95% *CI*: 0.81–0.89), and a similar prognosis was also observed for stage III (*HR* = 0.99; 95% *CI*: 0.95–1.03).[17]

Therefore, it is unclear whether the primary tumor location is related to DFS and OS among Chinese patients with stage II/III colon cancer. We used a single institutional Chinese database without racial diversity to examine the relationship between tumor site (right-*vs.* left-side) and 5-year mortality. Specifically, we sought to determine if this relationship is consistent across tumor stages.

Methods

Study population

All patients in this study underwent curative resection for colon cancer between January 2005 and December 2008 at the Cancer Hospital, Chinese Academy of Medical Sciences, Beijing, China. Histopathological staging was confirmed postoperatively by a consulting pathologist according to American Joint Committee on Cancer tumor-node-metastasis (TNM) staging system. To be eligible for the study, patients had