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Original article

C-reactive protein (CRP) as a prognostic factor for colorectal cancer after surgical resection of pulmonary metastases

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Keywords
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Summary

Introduction > Pulmonary metastases occur in up to 25% of colorectal cancer (CRC) patients. Many studies have reported that pulmonary metastasectomy might increase 5-year survival of these patients. The aim of this study was to describe our experience with pulmonary metastasectomy for metastatic colorectal cancer and to explore the prognostic value of serum C-reactive protein (CRP) and other factors.

Methods > Between June 2002 and December 2013, the clinicopathological data of 88 patients who underwent resection of pulmonary metastases from colorectal carcinoma were retrospectively reviewed and analyzed. Clinical, investigative and operative data were prospectively collected. Overall survival (OS) was calculated from resection of pulmonary metastases to death.

Results > There were 58 men and 30 women in this study, and their median age was 55 (range 31 to 85). Video-assisted thoracoscopic surgery (VATS) was performed in 59 cases (78%) and 29 patients (19%) underwent thoracotomy. Lung wedge resection and pulmonary lobectomy were performed in 52 (59.1%) and 36 patients (40.9%), respectively. Preoperative elevated CRP was present in 8 (9.1%) patients. After a median follow-up duration of 44 months, the cumulative 5-year survival was 45.4% and the median overall survival (OS) was 57.8 months. A significantly longer survival was observed in patients with normal preoperative CRP level compared with those with CRP level exceeding 10 mg/L (62.6 months vs. 34.3 months, $P = 0.011$). In multivariate analysis, preoperative CRP level was found to be independent significant prognostic factors for survival.

Conclusions > Pulmonary resection of metastatic colorectal cancer might offer a chance to prolong survival including those patients with extrapulmonary metastasis. Preoperative serum CRP level was identified as prognosis-related factor for surgery.

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Introduction

Colorectal cancer (CRC) is the third commonest malignancy worldwide [1]. Of that, around 5–25% of CRC patients will develop lung metastases at presentation or following colorectal surgery [2]. Due to the development of minimal invasive video-assisted thoracoscopy and the fact that liver metastasectomy contributes to survival improvement, pulmonary metastasectomy has emerged as a potentially curative option in the multimodal management of metastatic CRC [3]. The published 5-year survivals after pulmonary metastasectomy of colorectal origin can be elevated up to 62%, while that of patients without local treatment of pulmonary metastases was less than 5% [4]. Since the 1990s, several studies have looked for possible prognostic features indicating poor survival outcome and disease recurrence after pulmonary metastasectomy, such as metastases numbers, preoperative carcinoembryonic antigen serum (CEA) level, thoracic lymph node involvement and surgical procedures [5–8]. Infiltration of proinflammatory macrophages, cytokines and chemokines in the tumor microenvironment predispose the tumor to further progression, growth, invasion and metastasis [9]. The elevated CRP level, a major nonspecific systemic inflammatory marker, is associated with an increased risk of developing early recurrence and poor outcome following curative resection for colorectal liver metastases [9,10]. However, the relationship between elevated CRP and outcome in patients who had pulmonary resection is unclear. Therefore, the aim of this study is to explore the effects of preoperative CRP on CRC survival following pulmonary metastasectomy.

Patients and methods

Between July 2002 and December 2013, 88 patients underwent resection of pulmonary metastases from colorectal cancer. Each patient had a proven tissue diagnosis of metastatic colorectal adenocarcinoma. The criteria for resection of pulmonary metastases included unilateral or bilateral resectable lung lesions, no local recurrence of primary lesions, and adequate cardiorespiratory function for complete resection of all pulmonary lesions. Extrapulmonary metastases of little tumor burden were included. CRP measurements were taken on the day before surgery with none of the patients showing clinical signs of sepsis. Clinical, investigative and operative data were prospectively collected from computerized records. Follow-up data were obtained from patients' records and by contacting patients' respective general practitioners. The data were analyzed by SPSS 13.0 version. The prognostic effect of each variable on survival was evaluated using the Kaplan-Meier method and log-rank test. For the multivariate analysis of prognostic factors, the Cox mode was used. *P*-value of less than 0.05 was considered statistically significant.

Results

Patient characteristics

The study included 58 men (65.9%) and 30 women (34.1%), and the median age at time of diagnosis of CRC was 55 years (range 31 to 85 years). The primary tumor location included 25 (28.4%) colon and 63 (71.6%) rectum. Pulmonary metastasis was solitary in 71 patients and multiple in 17 patients (unilateral in 5, bilateral in 12). Five patients had extrapulmonary metastases, including 2 liver solitary metastases (1 of them had liver metastases resection after pulmonary metastasectomy), 1 thoracic lymph nodes metastases, 1 pelvic soft tissue metastasis and 1 pleura metastasis, and none of them received treatment of metastasis. Video-assisted thoracoscopic surgery (VATS) was performed in 59 cases (78%) and thoracotomy in 29 patients (19%). Fifty-two patients (59.1%) underwent lung wedge resection and 36 patients (40.9%) underwent pulmonary lobectomy (*table I*).

Preoperative CRP was elevated (> 10 mg/L) in 8 patients (9.1%). The differences in the clinicopathological features of patients with a normal CRP level compared with an elevated CRP are presented in *table II*. It showed that patients with an elevated CRP had no significant differences in different T or N stage of the primary tumor and site of the tumor.

Survival analysis

Median follow-up duration was 44 months (range 3 to 162 months). The median interval between CRC diagnosis to lung metastasis diagnosis was 25 months (range 0 to 122 months). After pulmonary metastasectomy, disease recurrence was identified in 26 of the 88 patients (distant metastasis in 7, local recurrence in 19). The median interval between pulmonary metastasectomy and disease recurrence was 13.5 months (range 4.2 to 34.8 months). At last follow-up, 51 patients (58.0%) were alive and the cumulative 5-year survival of all patients was 45.4%, and the median survival was 57.8 months.

Among the analyzed prognostic factors, age, gender, maximum tumor size of lung metastasis, localization of the primary tumor, metastases phases, number of lung metastasis, extrapulmonary metastases and preoperative CEA level did not influence survival significantly. However, a significant shorter survival was observed in patients with preoperative serum CRP level exceeding 10 mg/L compared with patients with normal level (34.3 months vs 62.6 months, $P = 0.011$) (*table I*) (*figure 1*). Furthermore, repeated analysis in patients with solitary or multiple lung metastases showed the prognostic value of CRP level. When assessing disease-free survival, patients with an elevated CRP had poorer survival compared with patients of normal CRP level, however, the survival difference was not significant (mDFI: 16.4 vs. 26.4 months, $P = 0.614$). Multivariate analysis further confirmed preoperative serum CRP level to be an independent significant prognostic factor for survival ($P = 0.016$).