

Survival Benefit of Palliative Local Treatments and Efficacy of Different Pharmacotherapies in Colorectal Cancer With Lung Metastasis: Results From a Large Retrospective Study

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Abstract

The role of palliative local treatments and the efficacy of different pharmacotherapies in colorectal cancer with initial lung metastasis was retrospectively investigated. Palliative local treatments resulted in better survival benefit than pharmacotherapy alone. First-line nonintensive pharmacotherapy showed similar survival durations compared to intensive regimens.

Background: For most colorectal cancer patients with initial lung metastasis (LM), the only suitable treatments are palliative, including palliative local therapy and pharmacotherapy. We investigated the role of palliative local treatments in prolonging survival and the efficacy of different pharmacotherapies. **Patients and Methods:** After performing a medical record review of 2233 patients with metastatic colorectal cancer, 684 were identified as having LM. Their clinicopathologic characteristics, treatment patterns, and outcomes were analyzed retrospectively. **Results:** For nonresectable initial LM, patients receiving palliative local therapy had significantly longer median progression-free survival (PFS) and overall survival (OS) than those treated with pharmacotherapy alone: PFS 16.1 months versus 7.4 months ($P < .001$) and OS 51.8 months versus 23.8 months ($P < .001$), respectively. Cox multivariate analysis confirmed the survival benefit induced by palliative local therapy. Chemonaive patients receiving single-agent fluoropyrimidine had shorter PFS and longer OS compared to oxaliplatin- or irinotecan-based doublets when used as first-line treatment (PFS 4.8, 7.4, and 7.3 months; and OS 28.7, 21.2, and 20.1 months, respectively); however, these differences were not statistically significant. The addition of targeted agents to cytotoxic drugs prolonged PFS (10.5 vs. 7.2 months, $P = .005$) but not OS (27.8 vs. 21.2 months, $P = .454$). Carcinoembryonic antigen level, LM-associated symptoms, extrapulmonary disease, and histopathologic type were independent pretreatment prognostic factors. **Conclusion:** Local treatments of LM may confer a survival benefit in the palliative setting. First-line single-agent fluoropyrimidine may be used in patients with good prognosis.

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Introduction

An increasing number of patients have been diagnosed with colorectal cancer (CRC) in the past few decades in China.¹ Approximately 50% of the CRC patients will develop metastatic

disease,² among which 29% will have initial lung metastasis (LM).³ However, the characteristics of LM have not been well studied.^{4,5}

Although not based on well-designed randomized clinical trials, radical lung metastasectomy is the recommended treatment approach for resectable LM with good prognosis and no extrapulmonary disease.^{6,7} Radiofrequency ablation and stereotactic body radiotherapy are alternative treatments in cases that are unsuitable for surgery.^{8,9} Among the initial LM population, 10% were suitable for radical therapy, while others were only eligible for palliative pharmacotherapy with or without local therapy.³

Pharmacotherapy is frequently used in clinical practice, but few data are available regarding the efficacy of chemotherapy, with or

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without targeted therapy. Some early studies suggested a better response and longer survival with the FOLFOX regimen (5-fluorouracil/leucovorin plus oxaliplatin) compared to FOLFIRI (5-fluorouracil/leucovorin plus irinotecan), but the differences were not significant.^{10,11} These studies were of great importance, but they failed to provide definitive recommendations on pharmacotherapy for LM. Moreover, the additional role of local therapy in the palliative setting has not been investigated.

We retrospectively investigated the characteristics of CRC patients presenting with initial LM, clarified the impact of palliative local treatments on survival, and explored the efficacy of chemotherapy with or without targeted agents.

Patients and Methods

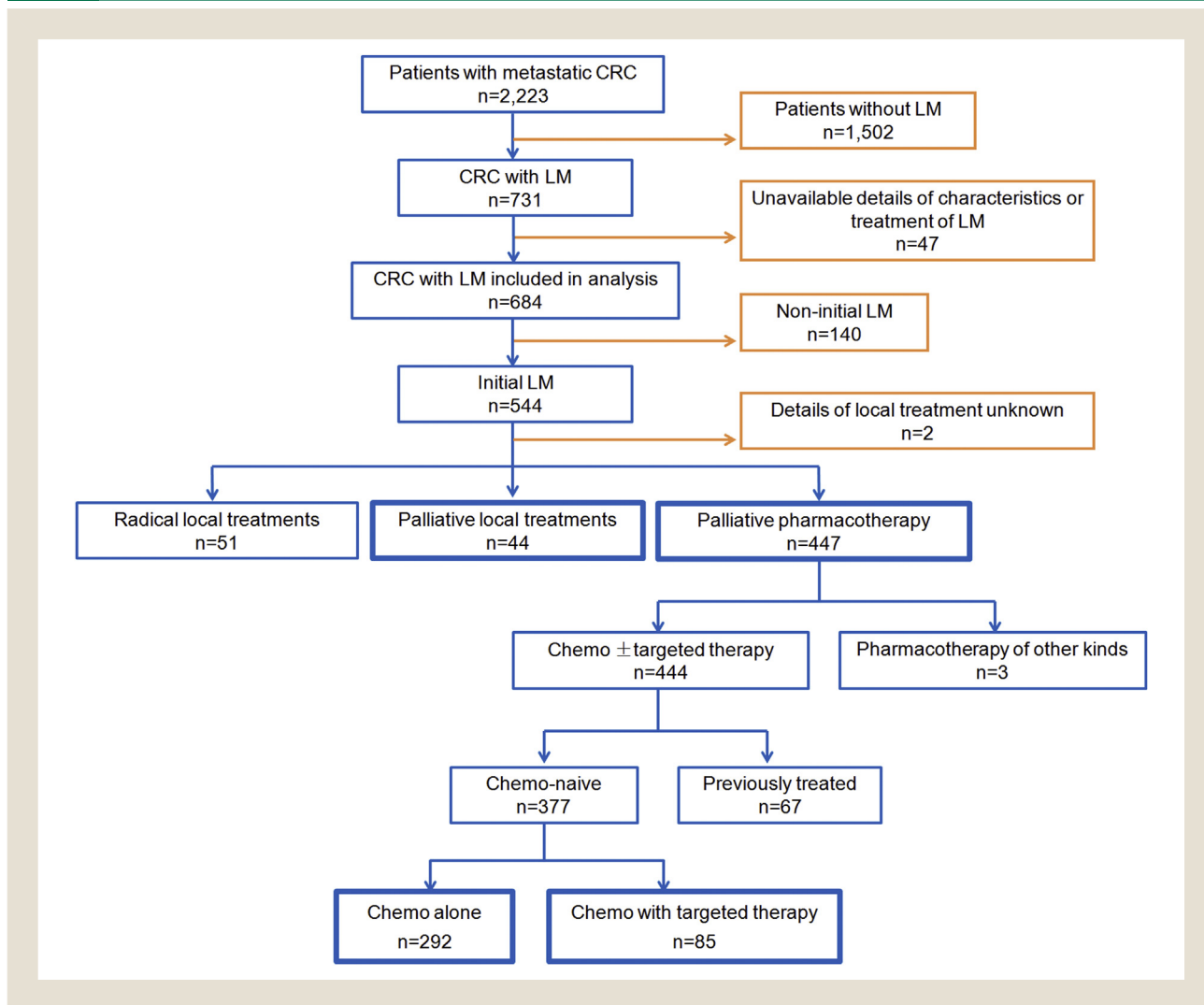
Patients

A total of 2676 medical records of CRC patients who were treated in the Department of Gastrointestinal Oncology, Peking University Cancer Hospital and Institute, from January 1, 1996, through April 1,

2017, were reviewed. Of these, 2233 metastatic cases were identified, and among these, 731 patients were diagnosed with LM on the basis of chest computed tomographic scan or positron emission tomography–computed tomographic scan. LM was confirmed pathologically if necessary. After excluding the cases without sufficient details of characteristics or treatment, a total of 684 LM patients were included in the study. Patients' clinicopathologic and genetic characteristics were extracted from clinical records for each case. Initial LM was defined as LM that occurred as the first evidence of metastasis, and isolated LM was characterized by the absence of extrapulmonary metastasis. This study was approved by the Beijing Cancer Hospital ethics committee (no. 2017KT90). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Outcomes and treatments for non-initial LM patients were greatly influenced by previous treatments for prior metastasis; this population

Figure 1 Flow Diagram of Patient Selection



Abbreviations: CRC = colorectal cancer; LM = lung metastasis.

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