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Original research

Risk factors for the development of metachronous bone metastasis in colorectal cancer patients after curative resection

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HIGHLIGHTS

- Most colorectal cancer patients with bone metastasis have other metastases at the same time.
- The value of PET-CT in colorectal cancer patients' follow-up is still controversial.
- Tumor location and lymph node involvement are independent risk factors for the development of bone metastasis.

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ABSTRACT

Objective: Metachronous bone metastasis (MBM) occurs in 6–10% of colorectal cancer (CRC) patients following surgical treatment. The aim of this study is to determine the risk factors affecting the development of MBM in CRC patients following curative resection.
Method: Clinical and pathological records of 516 CRC patients who underwent curative resection were retrospectively studied. The association between clinicopathological variables and development of MBM was investigated using univariate and multivariate analyses.
Result: The incidence of MBM was 6.0% and the median time of developing MBM was 15 (range, 1–89) months. Univariate analysis identified that lymph node involvement ($p = 0.001$), tumor stage ($p = 0.020$) and tumor location ($p = 0.015$) were significantly correlated with development of MBM. Multivariate analyses showed tumor location ($p = 0.039$) and lymph node involvement ($p = 0.003$) were independent risk factors contributing to the occurrence of MBM.
Conclusion: This study indicated that tumor location and lymph node involvement were independent risk factors for development of MBM in CRC patients after curative resection.

1. Introduction

Colorectal cancer (CRC) is the third most common cancer worldwide in males and the second in females, with an estimated 1.2 million new cases diagnosed per year [1]. To date, surgical resection offers the only chance for potential curative therapy. However, even after radical surgery, more than 30% CRC patients develop metastases [2]. Common sites of metastases from CRC include liver and lung while metachronous bone metastasis (MBM) occurs infrequently and is indictable of poor patient prognosis [3–6].

In recent years, there is an increase in the number of publications in which CRC patients with MBM are analyzed [6–8]. However, there is still no definite predictive factor for MBM in patients with colorectal cancer. In the present study, we retrospectively analyzed patients who underwent curative surgery for CRC in our hospital with the aim of identifying possible risk factors for the development of MBM.

2. Method

This is a retrospective study of medical records, with prospective collection of patients' data in a computerized database recording all the preoperative, peri- and postoperative information. 594 consecutive CRC patients received surgeries in Changzheng hospital between May 2004 and December 2009. Eligibility criteria: 1. All included patients had historically confirmed colorectal

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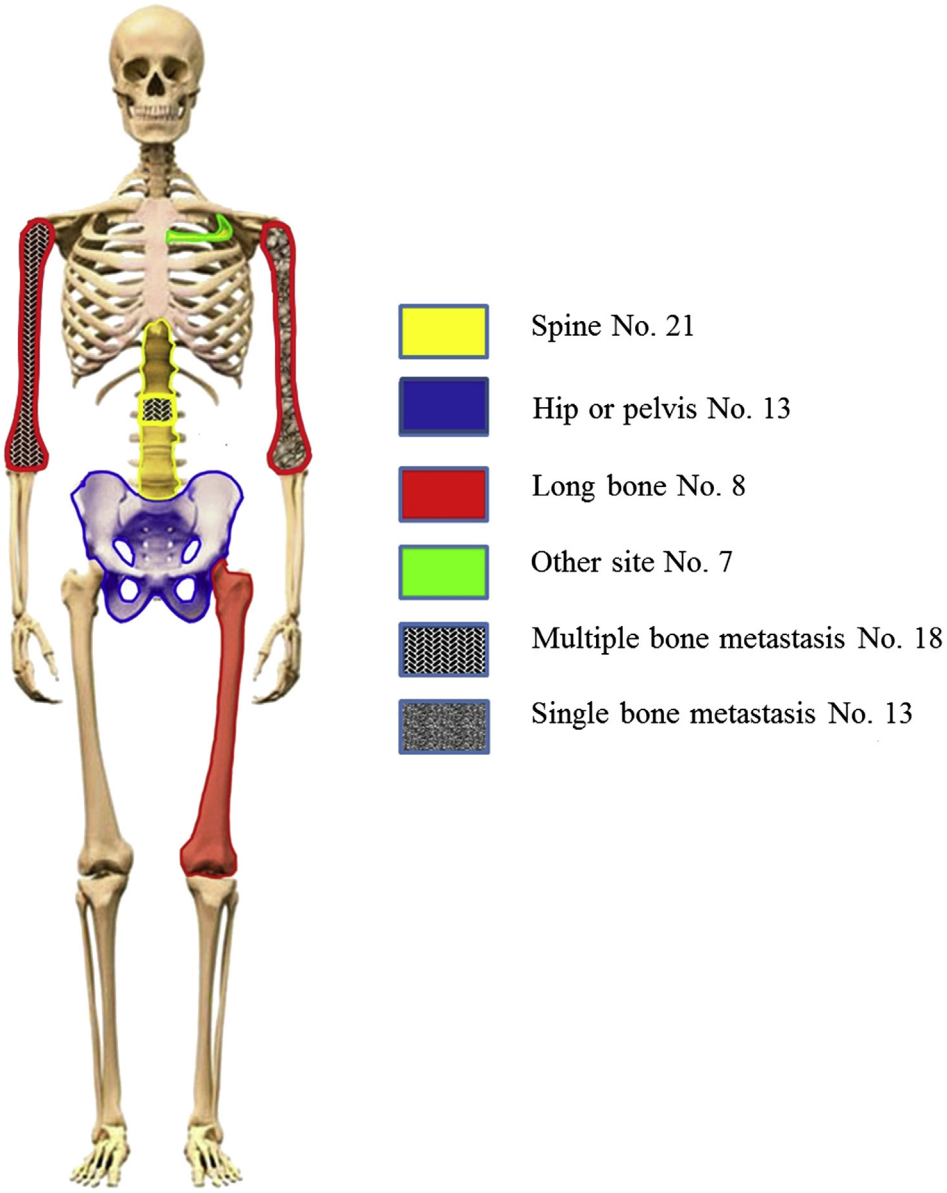

Fig. 1. Patterns of MBM in CRC patients following radical resection.

adenocarcinoma and received radical surgery (R0). 2. For patients with radical surgery, the resection margins were historically free of diseases and regional lymph nodes were dissected according to guideline. 3. Patients with bone metastasis at diagnosis were excluded. 4. Patients with primary cancer in another organ were excluded. Tumor stage was assigned to each patient according to the AJCC guideline (American Joint Committee on Cancer, 6th edition) [9]. Lymph node involvement was divided into N0, N1 and N2 based on AJCC. All stage III and IV patients received neoadjuvant chemotherapy based on the Clinical Practice Guideline in Oncology version 2006 (National Comprehensive Cancer Network, NCCN). The neoadjuvant chemotherapy will not be considered as a comparative factor in subsequent analyses, because it is strongly associated with tumor stages. According to the NCCN guideline, all CRC patients in stage II or more advanced CRC received a 5-Fu-based chemotherapy for at least 8 cycles postoperatively.

59 patients were treated with palliative surgery, and were excluded. The rest patients were followed-up until death or until April 2013. 19 patients were lost at follow-up. Finally 516 CRC patients were included in this study. The time of follow-up was calculated from the day of surgery to death or April 2013. Overall survival of MBM patients was calculated from the time of radical colorectal surgery. Kaplan Meier curves for MBM and none MBM patients were performed.

Bone metastasis was defined with the physician report, a positive bone scan or identification of bone metastasis by other assessment such as X-ray, computed tomography (CT) scan or magnetic resonance imaging (MRI).

During the follow-up, every patient underwent a bone scan each year to detect bone metastasis. For patients with skeletal related events (SREs; defined as pathological fracture, spinal cord compression, bone pain, radiotherapy or surgery for bone lesion and hypercalcemia of malignancy), related examinations were performed to make sure if they developed bone metastasis.

Medical records of included patients were reviewed to collect the following information: age, sex, hemoglobin at admission,