Introduction

Postoperative recurrences including local and distant metastases often occur in colorectal cancer patients who underwent curative surgery. Isolated paraaortic lymph node metastasis or peritoneal dissemination as first site of recurrence after surgery is relatively uncommon, accounting for nearly 1% and 5% of all, respectively. Paraaortic lymph node recurrence is usually accompanied by metastasis to other organs. However, localized and resectable isolated paraaortic lymph node recurrence has the potential of long-term survival by curative resection. In contrast, the efficacy of resecting peritoneal recurrence has not been proved. However, curative resection is sometimes considered after systemic chemotherapy for localized peritoneal recurrence. Moreover, attempt of complete cytoreductive surgery with hyperthermic intraperitoneal chemotherapy for peritoneal recurrence has been reported centering on European countries in years.

In either type of recurrence, early detection is necessary to allow for treatment of the recurrent tumor. Therefore, it is important to clarify the risk factors for these recurrences. In this study, we have evaluated the risk factors for isolated paraaortic lymph node or peritoneal recurrence after curative surgery in patients with colorectal cancer in a pooled analysis of large three randomized control studies.

Patients and Methods

Clinical trial data from Japanese Foundation for Multidisciplinary Treatment of Cancer (JFMC) studies 7, 15 and 33 were pooled for this analysis, providing a total number of 5530 patients. The key findings of each trial had been published by peer review journal. In the JFMC 7 and 15, patients with advanced colorectal cancer were randomly allocated to adjuvant oral 5-fluorouracil and
observation after surgery\textsuperscript{3}. In the JFMC 33 trial, patients with advanced colorectal cancer were allocated to adjuvant tegafur / leucovorin after surgery for 6 months or 18 months\textsuperscript{4}.

We extracted the patients with isolated paraaortic lymph node metastasis or peritoneal dissemination as first site recurrence after surgery from the database of each trial.

**Statistical methods**

Statistical analyses were performed using SPSS Version 19 software (SPSS Inc., Chicago, USA) and SAS version 9.4 (SAS Institute Inc., Cary, NC). The clinical and pathological variables were compared by the chi-square tests for categorical variables and t-test for continuous variables. The hazard ratio was calculated in uni- and multivariate analyses using Cox proportional hazards regression models. In all analyses, statistical significances were defined as p-value < 0.05.

**Ethics**

This study was conducted in accordance with the ethical principles that had their origins in the Declaration of Helsinki, and approved by the institutional review board of JFMC.

**Data collection and analysis**

Each trial data collection and analyses regarding clinicopathological parameters, recurrent status and survival outcome have been finished. Details of the more scrutinized findings of this pooled analysis will be published elsewhere after a careful review of the integrated data.

**Disclosure Statement**

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**References**

1) Jayne, D.G., S. Fook, C. Loi, and F. Seow Choen. (2002) Peritoneal carcinomatosis from colorectal cancer. Br. J. Surg. 89: 1545-1550.
2) Min, B., N. Kim, S. Sohn, C. Cho, K. Lee, and S. Baik. (2008) Isolated paraaortic lymph-node recurrence after the curative resection of colorectal carcinoma. J. Surg. Oncol. 97: 136-140.
3) Hamada, C., J. Sakamoto, T. Satoh, S. Sadahiro, H. Mishima, K. Sugihara, S. Saji, and N. Tomita. (2011) Does 1 year adjuvant chemotherapy with oral 5-FUs in colon cancer reduce the peak of recurrence in 1 year and provide long-term OS benefit? Jpn. J. Clin. Oncol. 41: 299-302.
4) Sadahiro, S., T. Tsuchiya, K. Sasaki, K. Kondo, K. Katsumata, G. Nishimura, Y. Kakeji, H. Baba, S. Sato, K. Koda, Y. Yamaguchi, T. Morita, J. Matsuoka, H. Usuki, C. Hamada, and S. Kodaira. (2015) Randomized phase III trial of treatment duration for oral uracil and tegafur plus leucovorin as adjuvant chemotherapy for patients with stage IIIB/III colon cancer: final results of JFMC33-0502. Ann. Oncol. 26: 2274-2280.