Dr. Masaki Hashimoto: clinical impact of circulating tumor cell in metastatic colorectal cancer patients who underwent pulmonary metastasectomy

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Expert introduction

Dr. Masaki Hashimoto, MD, PhD is the Assistant Professor of Thoracic Surgery at Hyogo College of Medicine and a member of the European Society of Thoracic Surgeons. Dr. Hashimoto received his medical degree from Hyogo College of Medicine. His general, cardiovascular and thoracic surgical training were all completed at Hyogo College of Medicine Hospital. He has a rich surgical experience in lung cancer and mesothelioma. Dr. Hashimoto focuses his research interests on the clinical use of circulating tumor cells and development of new ways to test and treat malignant pleural mesothelioma.

Figure 1 Dr. Masaki Hashimoto, MD.

Editor's note

Dr. Masaki Hashimoto, MD is Assistant Professor of Thoracic Surgery at Hyogo College of Medicine (*Figure 1*).

Dr. Hashimoto's paper entitled "Clinical Impact of Circulating Tumor Cell in Metastatic Colorectal Cancer Patients Who Underwent Pulmonary Metastasectomy" was accepted for presentation at the 25th Annual Meeting of European Society of Thoracic Surgeons (ESTS) held from 27–31 May in Innsbruck, Austria. Before the opening of ESTS annual meeting, the academic journalist Dr. Qiuyuan Li raised five questions related to the presented research and conducted an interview with Dr. Hashimoto through email, discussing some details about circulating tumor cell (CTC) testing and the clinical impact of CTCs in his study.

Interview topics

Q1: How many patients received pulmonary metastasectomy in your study and what was the surgical extent?

Total of 79 patients were enrolled in this study, but 6 patients were excluded from analysis due to incomplete resection. We analyzed the clinical impact of CTC in the remained 73 patients. Regarding the surgical procedure in this study, partial resection was the principle in our institution basically, but segmentectomy or lobectomy was performed based on some kinds of variables, such as the number of tumor, the location of tumor, the size of tumor and so on. Among the 79 patients, partial resection was only performed in 42 patients, segmentectomy was in 10, lobectomy was in 21, and completion pneumonectomy was in 1, respectively. Lymph node dissection was only performed in patients with suspicious of lymph node metastasis.

Q2: What was the timing of circulating tumor cell (CTC) testing in your study? Was the test serial or one-time only for each patient?

In this study, CTC testing was performed only one time. We took a 7.5 mL of peripheral blood just before operation. The aim of this study was to assess the CTC-count as a prognostic factor in metastatic colorectal cancer (mCRC) patient who undergoing pulmonary metastasectomy. We assessed CTC-count not only for prognostic factor but also for surgical criteria of pulmonary metastasectomy. Regarding surgical criteria, CTC-count should be assessed

preoperatively. Although postoperative CTC-count may predict postoperative survival as well as other malignancies, it will be influenced by surgical procedure or surgical manipulation. Based on these reasons, CTC-testing was performed only before surgery.

In addition, the CTC-count was evaluated after surgery by only two researchers (Kazue Yoneda and Fumihiro Tanaka). They evaluated the CTC-count without any knowledge of clinical characteristics of patient.

Q3: What tool did you use to test for CTCs?

We evaluated CTC using CellSearch system (Veridex LLC) in this study. CellSearch system was able to detect CTC semi-automatically. The principle of CellSearch system was as follows: in brief, CTCs were immune-magnetically captured using ferro-particles coupled to a monoclonal antibody against the epithelial cell adhesion molecule (EpCAM), and the CTCs-enriched samples were then stained with 4',6-diamidino-2-phenylindole (DAPI) and an anti-cytokeratin antibody conjugated with phycoerythrin (CK-PE). Contaminated white blood cells were excluded by negative selection for CD45. Stained cells were then analyzed on a florescent microscope using the Cell track Analyzer II (Veridex LLC). The criteria for each cell to be defined as a CTC are as follows: round to oval morphology, a visible DAPI-positive nucleus, positive cytokeratin staining in the cytoplasm, and negative staining for CD45. All evaluations were performed without knowledge of clinical characteristics of patients. The number of CTCs per 7.5 mL of peripheral blood was represented as the CTC-count.

Q4: What was your finding regarding the clinical impact of CTCs in the study setting? Were there other positive impact factors aside from that of CTC?

We found that CTC-count was a prognostic factor in mCRC patient who underwent pulmonary metastasectomy through this study. Briefly, significant short disease free survival (DFS) was observed in patients with 2 or more CTC-count. In contrast, significant correlation between CTC-count and overall survival (OS) was not observed in this study. OS would be affected by various factors including chemotherapy. As advanced chemotherapy for mCRC, 5-year survival rate has recently been up to 60%. These results would suggest that CTC would be a surrogate marker of undetectable distant metastasis via conventional radiological examination.

In this study the serum level of CEA was also prognostic factor in mCRC patient who underwent pulmonary metastasectomy. The preoperative serum level of CEA was significantly correlated with short DFS and OS. Many literatures also reported the serum CEA level as a prognostic factor, the result of this study was also similar with previous reports.

Q5: Could you speculate the mechanism by which some patients would develop a favorable CTC profile, and how can we utilize the mechanism in the future?

In this present study, most of patient was favorable group (CTC-count <2), and CTC was not observed in 60 patients (82.2%). It suggested that most of patients in this study might be "local disease", and our surgical criteria might be also justified regarding of CTC-count. This study suggested that undetectable distant metastasis would be existed in mCRC patient with 2 or more CTCs As a result of this study, CTC-count may be useful as an exclusion criterion for pulmonary metastasectomy in mCRC patients.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

(Section Editor: Qiuyuan Li)

Author/Academic journalist: Qiuyuan Li, MD. Department of Thoracic Surgery, Tongji University, Shanghai, China. Mr. Qiuyuan Li is a predoctoral student of medical school of Tongji University, who majors in thoracic surgery and has been a visiting graduate student of Mayo Graduate School affiliated to Mayo Clinic during 2016 and 2017. His primary work lies in clinical big data analysis and epigenetic study of lung cancer. His publication includes 2 articles in the Chinese Journal series and 1 original article in *European Journal of Cardio-Thoracic Surgery* (Accepted). He has taken part in the editing and translation of 2 books in his academic area, and had delivered 1 oral presentation in an international conference.

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