Factors Affecting the Outcome of a Pulmonary Resection for Metastatic Colorectal Cancer: Efficacy and Pitfalls

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Pulmonary resection of metastatic colorectal cancer is widely practiced in the field of oncologic surgery. However, only a highly selected subset of patients is eligible for resection, and the average recurrence rate is still high. According to general guidelines proposed by the UK National Institute for Clinical Excellence [1] and the National Comprehensive Cancer Network [2], however, for the following cases of metastatic pulmonary lesions, surgery is indicated:

1) the metastases seem to be technically resectable,
2) the general and functional risks are tolerable,
3) the primary tumor is controlled, and
4) no extrathoracic lesions are detected (with the exception of hepatic lesions for which both the hepatic and the pulmonary metastases can be completely removed).

According to a review of the literature on surgical management of a pulmonary metastasis of colorectal cancer, the results vary depending on the selection criteria of individual surgeons or institutions. Due to the problems associated with a lack of randomized, prospective clinical studies, it remains difficult from an evidence-based perspective to assess or summarize the clinical usefulness of surgical management for metastatic lesions [3]. To date, however, most of the retrospective studies have demonstrated that a surgical resection of the pulmonary metastasis of colorectal cancer is a safe treatment modality with a lower degree of mortality.

The following meta-analysis for a pulmonary metastasectomy in cases of colorectal cancer showed that for all 1,307 patients investigated, a minimum number of 40 cases with a mean fol-

low up of 37.6 months, the overall 5-year survival was 40-68% after complete surgical resection, and the mean 5-year disease-free survival after complete resection was 19.5-34.4%. Recent reports reflect better treatment outcomes, but not come to the of all the patients [4]. Traditional risk factors and selection criteria are currently being discussed, but decision making presupposes a personalized strategy with predictive models. Such predictive models have a number of uses. In particular, due to the selection of patients who might benefit from such treatment modalities as neoadjuvant chemotherapy prior to a prethoracotomy, surgery, or active chemotherapies, those with good prognostic factors can receive the surgical treatment at earlier times and those with a poor prognosis are subject to delayed surgery. This delay, or "trial of time," can allow a better assessment of additional disease and provide time for neoadjuvant therapy or more aggressive adjuvant therapy. Further, it can also be used to enroll patients who are at increased risks of recurrence in prospective randomized trials and can provide a postoperative surveillance strategy following the actual surgery [5].

On a multivariate analysis, Kanemitsu et al. [6] maintained that five prognostic factors, the primary histology, hilar or mediastinal lymph node involvement, the number of metastases, the preoperative level of the carcinoembryonic antigen, and extrathoracic disease, would be risk factors. These factors have a prognostic value for long-term survival, and related study models are advantageous in that the degree of clinical applicability is relatively higher. In addition, other prognostic factors affecting the survival rate following the pulmonary resection include a disease-free interval during which a diagnosis of pulmonary lesions is made. As shown in this study, however, there was no significant difference.

In recent years, as a prognostic factor for pulmomary metastasis, genetic tests based on such technologies as the Affymetrix Gene Chip microarray have been applied. However, because of the prohibitive costs, reliance on frozen tissue, and advanced technical expertise required to use the technology, it is debatable whether such tests will ever be clinically applicable [7]. Thus, the immunohistochemical (IHC) staining profile can be a useful surrogate for gene expression analysis. Many studies

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have focused on the correlation between histopathologic and IHC measurements and survival [8, 9]. According to Shiono et al. [9] the histopathologic features of pulmonary metastases in 87 patients revealed the morphologic feature of an aerogenous spread with floating cancer cell clusters and vascular invasion at metastatic sites to be a prognostic factor of significance for survival. Lymphatic invasion or microsatellite instability of the primary tumor, however, has been reported to be unrelated to survival. Although smaller in number, with the recent advancement in molecular biological methods, ongoing studies are being conducted to examine the pulmonary metastasis of colorectal cancer. These studies will provide us further understanding of pulmonary metastatic cascade and allow patient treatment to be personalized.

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