Circumferential resection margin in esophageal cancer

In 1993, Sagar et al. reported that microscopic involvement of the circumferential resection margin (CRM) is related to local recurrence and decreased survival. Since then, the role of the CRM in esophageal cancer has been extensively investigated in the literature. Dexter et al. in 2001 found in their study, which included 135 patients with esophageal cancer, that 64 patients (47%) were positive CRM and the presence of tumor within 1 mm of the CRM is an independent prognostic factor for esophageal cancer. In 2006, Griffiths et al. also reported that CRM involvement predicted poor prognosis in patients with resected esophageal cancer. In a recent study focusing on the significance of CRM involvement in 94 patients who underwent neoadjuvant chemoradiation followed by surgery, Liu et al. concluded that the involvement of CRM is a significant risk factor of survival. Of these 94 patients with squamous cell carcinoma of the esophagus, 17 had positive CRM and 7 had T4 tumor. However, in contrast to these reports, some authors have suggested that CRM is not a prognostic predictor in esophageal cancer.

The most important predictors of esophageal cancer prognosis include the overall TNM stage, completeness of resection (R classification), and status of lymph node metastasis. Prior to discussing the importance of CRM in esophageal cancer, the relationship between residual disease classification and CRM should be clarified. The residual tumor classification is a strong prognostic factor after surgical resection in esophageal cancer. It is defined such that R0 is complete resection, R1 is residual microscopic disease, and R2 is macroscopic disease. Usually, the CRM is defined as the surgically cut surface of the connective tissues that encase the esophagus. To investigate the significance of CRM in the prognosis of the patients with esophageal cancer, patients with incomplete resection should not be included. In the assessment of CRM in esophageal cancer specimens, according to the College of American Pathologists (CAP), the R1 category is considered to include only tumors positive at the cut margin of resection. However, the Royal College of Pathologists (RCP) considered that the R1 category as tumor is located within 1 mm of the cut margin. Most studies investigating the association between CRM involvement and survival in esophageal cancer did not address the differences between the CRM definitions of these two schools. In 2009, Deeter et al. analyzed 135 patients with T3 esophageal cancer. They found that positive margins were identified in 16 cases in the CAP group, and in 83 cases in the RCP group. Only R1 margins in the CAP group were associated with survival. The authors concluded that positive CRM is important in predicting survival, and the CAP criteria provide a more clinically meaningful assessment. Similar results were obtained by Verhage et al. The authors evaluated the significance of these two criteria on survival in T3 adenocarcinoma of the esophagus and found that there were more patients with positive CRM according to RCP criteria; however, the difference of survival between positive and negative CRM involvement was not significant in RCP criteria for these patients. They concluded that positive CRM according to CAP criteria is a strong independent prognostic factor for patients with T3 adenocarcinoma of the esophagus. Recently, Rao et al. reported that there was no survival difference between patients with resection margin involvement, and margins from 0.1 mm to 1 mm. They suggested that a resection margin >1 mm can provide better survival in patients undergoing esophagectomy for esophageal cancer.

Regarding the effect of chemoirradiation on the CRM, in 2004, Mulligan et al. advocated that multimodal therapy reduced the involvement of margin in esophageal cancer. However, the definition of margin involvement was not mentioned in the study. In 2008, Sujendran et al. studied the significance of CRM in 242 patients who underwent esophagectomy, including 142 patients who underwent neoadjuvant chemotherapy. Positive CRM was considered as tumor identified microscopically within 1 mm from the resection margin. They concluded that a positive CRM is an independent predictor of overall survival after esophageal cancer resection, and there was a significant decrease in CRM involvement with the induction of neoadjuvant chemotherapy. In contrast to that report, Harvin et al. recently studied 160 patients having neoadjuvant chemoradiotherapy followed by surgery for esophageal adenocarcinoma and found that involvement of CRM was not a significant predictor of survival in these patients. In 2011, Chao et al. from Taiwan investigated the impact of CRM distance on local recurrence and survival after chemoradiotherapy in squamous cell carcinoma. They selected 151 patients with T3 disease of squamous cell carcinoma and found that CRM involved by tumor is an indicator of both local and distant recurrence, whereas CRM involved by tumor <1 mm was only associated with local recurrence. It is interesting to note that in the study of Liu et al. under the
same definition, the incidence of positive CRM was much lower than that in the series from Chao et al.13 (18.1% vs. 51%). In the series of Liu et al.,4 patients with T4 tumor were also included and whether or not complete resection was achieved in these cases was not mentioned in the study. Actually, according to the literature, the percentage of CRM involvement in esophageal cancer varied in different reports. It is recommended that to interpret the significance of CRM involvement in esophageal cancer, the involvement of CRM should be defined clearly in the study. It is possible that the prognostic impact of CRM status is simply related to the completeness of the surgical dissection for esophageal cancer.

In conclusion, for patients with esophageal cancer, tumor involvement at resection margin is associated with poor prognosis, which in part may be due to incomplete resection. For cases with tumor involvement <1 mm from the CRM but not at the margin, the prognostic impact of CRM involvement needs to be investigated further. For cases with tumor involvement >1 mm from the margin, the prognosis seems to be better than cases with tumor involvement <1 mm from the CRM. Thus, to assess the impact of CRM involvement for patients with esophageal cancer, enrolled patients should have at least complete resection without macroscopic residual tumor during operation, and the definition of the CRM involvement should be clearly mentioned in the study. Moreover, to obtain accurate report of involvement of the CRM, careful examination of the esophageal resection specimen should be fully completed.

References


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