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Commentary: How to evaluate the effect of neoadjuvant therapy for esophageal cancer? More studies are still needed

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In the Chemoradiotherapy for Oesophageal Cancer Followed by Surgery Study (CROSS), pathologic complete response was observed in 28 of 121 patients with adenocarcinoma (23%), and 18 of 37 with squamous-cell carcinoma (49%), the survival benefit was more pronounced in patients with esophageal squamous cell carcinoma.¹ However, the characteristics of residual tumors were not fully investigated in the CROSS study.

In a cohort of patients with esophageal squamous cell carcinoma after neoadjuvant chemoradiotherapy (nCRT), Tang and colleagues² present the pattern of residual tumors into 4 types: I, regression toward the lumen; II, regression toward the invasive front; III, concentric regression; and IV, scattered regression. Moreover, the frequency of pathological complete response was lower in the lymph nodes (29.2%) than in primary lesions (33.6%). According to the pattern of tumor regression and amount of the residual tumors, 62.7% could not be detected due to potentially negative biopsy in the superficial layer. Based on pathology results, the authors investigated the characteristics of tumor regression after nCRT, offering novel information for the treatment of esophageal cancer after nCRT. However, a clinical question arises: How to predict the type of tumor regression by preoperative workup?

The relation between clinical and pathologic tumor responses is crucial in treatment decision making for patients with esophageal cancer. To evaluate the effect of neoadjuvant therapy, the Detection of Residual Disease After Neoadjuvant Chemoradiotherapy for Oesophageal Cancer

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CENTRAL MESSAGE

More work is needed to increase the accuracy of preoperative evaluation for esophageal cancer. The treatment decision should be made for the best survival.

(preSANO) study was initiated to evaluate the accuracy of different diagnostic techniques for clinical response evaluations. However, with the combination of endoscopic ultrasonography, bite-on-bite biopsies, and fine-needle aspiration, 25 of 47 tumor regression grade (TRG) 1 or 2 tumors (53.2%) and 4 of 41 TRG 3 or 4 tumors (9.8%) were still missed.³ Thus, more work is needed to increase the accuracy of disease evaluation, particularly for TRG 1 or 2 patients.

Regarding the treatment decision after nCRT, the optimal strategy should be made for a better survival, which is the most important outcome. For this aim, the ongoing Surgery as Needed Approach in Oesophageal Cancer Patients (SANO) trial compared active surveillance with standard resection for patients who achieve a complete response after nCRT,⁴ and active surveillance could be a kind of standard care if this strategy leads to noninferior survival.

Due to the difficulties in tumor regression evaluation, on the other hand, compared with neoadjuvant therapy, postoperative adjuvant therapy was delivered based on accurate pathological staging rather than inaccurate clinical staging. In the trial comparing esophagectomies via right and left thoracic approach, which was performed under the policy of surgery plus adjuvant therapy, 5-year overall survival was 63% after esophagectomy with radical 2-field lymphadenectomy via right thoracic approach, and 51% for those with lymph node metastasis.^{5,6} Thus, new trials comparing neoadjuvant and adjuvant treatment for esophageal squamous cell carcinoma are needed.

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More work is needed to increase the accuracy of clinical disease staging and evaluation of tumor regression response. For patients with esophageal cancer, the optimal treatments should be established based on prospective evidence with the best outcomes.

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