

Nodal status is best predictor of outcome after neoadjuvant therapy for esophageal cancer

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The number of lymph nodes that contain evidence of cancer is the best predictor of the effectiveness of adding chemotherapy and radiation to a treatment plan prior to surgery in individuals with oesophageal cancer, according to a study published last month in the *Annals of Surgery*. The authors say their finding is particularly important because the focus of recent pathological studies of response to neoadjuvant therapies has been on the primary tumour rather than nodal sites.

Multimodal neoadjuvant therapy---where suitable patients are given several cycles of drugs and radiation therapy before undergoing surgical procedures to remove their tumour---is increasingly being used by oncologists as a way to boost survival rates from oesophageal cancer which, even with the most radical surgery, remain low: only 50% of patients survive for 3 years. However, the evidence for which additional therapies work best is confusing and conflicting. What is more, although it is widely accepted that there is a group of patients in whom this approach works well, identifying who these patients are is no easy task.

To help find ways of pinpointing individuals who might respond best to neoadjuvant treatment, John Vincent Reynolds and colleagues followed the progress of 243 patients who were treated with chemotherapy and radiation before surgery over 5 years. They paid particular attention to the histomorphological responses of patients---changes in the structure and appearance of tissue samples when viewed under a microscope---in

addition to assessing prognosis using the traditional TNM method of staging, which takes into account tumour size, involvement of lymph nodes (nodal status), and presence or absence of metastases.

The study group consisted of all patients undergoing neoadjuvant treatment for oesophageal cancer at St James' Hospital in Dublin, Ireland. Patients with oesophageal cancer were deemed suitable for multimodal therapy if they fulfilled a list of pre-set criteria, including being younger than 77 years, fit for surgery, and having a tumour of resectable size and location. The patients were given a standard protocol of radiation therapy and concurrent chemotherapy with fluorouracil and cisplatin before undergoing thoracotomy with lymphadenectomy and nodal dissection; the extent of surgery and lymph node dissection depended on the exact location of the tumour. 30 patients did not proceed to surgery because of disease progression or deterioration in performance status.

Several tissue samples from each patient were extracted during surgery and were subsequently examined for extent of residual cancer, depth of invasion, and lymph node metastasis. The patients were also assigned a tumour stage according to the TNM staging system. All patients were followed up with 6 monthly endoscopy and annual CT scans.

Of the 213 patients who underwent surgery, 41 (19%) had a complete pathological response to the pre-surgery therapy, meaning there was no sign of cancer in the tissue samples. 31 (15%) of the remaining patients were classed as having stage 1 disease (the least advanced), 69 had stage 2 disease, and 72 (35%) had stage 3 disease. After a median follow up of 60 months, median survival for the whole group was 18 months. But for the group of patients who achieved a complete pathological response, 5-year survival was 50%, with median survival of 56 months. "The achievement of a complete pathologic response following neoadjuvant chemotherapy alone or in combination with radiotherapy for oesophageal tumours is a surrogate marker of survival advantage,"

explain the authors.

However, the study established that it was nodal status rather than attainment of pathological response that was the most significant determinant of prognosis. When individuals with complete pathological responses were compared with those who had no nodal involvement after neoadjuvant therapy, there was no significant difference in the 1, 3, and 5 year survival rates. And within the node-negative group, the combination of complete response with a low tumour stage conferred better survival: individuals with stage 1 disease and no involved nodes (n=65) had a median survival of 67 months and 5-year survival of 53%, compared with 25 months and 30% for people with stage 2 and 3 tumours and no nodal involvement after neoadjuvant treatment. Interestingly, pretreatment clinical stage had no predictive value on histomorphological response.

The authors concluded that because the study suggests nodal status after neoadjuvant treatment is the strongest determinant of outcome, there is no evidence that an assessment of histomorphological response should be incorporated into a revised TNM system or that traditional methods of assessing prognosis should be altered. However, they added, histomorphological response might be a surrogate for nodal status and residual tumour volume therefore presenting the option of a non-operative approach in cases where the likelihood of nodal disease is small. According to the authors, the study also raises the question that if patients have no nodal involvement is neoadjuvant chemoradiotherapy justified at all"

Source: European School of Oncology

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