



Intensive Surveillance After Esophagectomy in Patients with Esophageal Cancer: When, Why, and How Often?

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Currently, curative treatment of patients with esophageal cancer consists of neoadjuvant treatment with chemoradiotherapy, followed by surgical resection.^{1,2} Since last year, adjuvant nivolumab has been added to the regimen in patients who had a radical resection with residual disease in the pathology report.³ In addition, several trials using targeted drug therapy and immunotherapy are ongoing, but mainly still in the palliative setting.⁴ Although addition of immunotherapy significantly improves the disease-free survival in these patients and thereby probably also the long-term survival, prognosis is still poor since a relative high number of patients curatively treated develop recurrent disease and will eventually die. Given the high number of recurrent disease, it seems logical to perform surveillance in these patients. However, despite ongoing discussion in past decades, there is still no consensus on how to monitor these patients postoperatively, or at all. In some centers routine surveillance and imaging is standard, while in others only symptom-triggered surveillance is performed and the outpatient visits focus on functional complaints and quality of life.

Takeuchi et al. described a retrospective study on intensive imaging surveillance in patients operated on for esophageal cancer.⁵ In this Japanese study, > 90% of patients had squamous cell carcinoma. Routine postoperative surveillance consisted of a 3–6-month interval outpatient clinic visit, thoracoabdominal CT, and esophagogastroduodenoscopy. Their main conclusion was that

recurrence can be detected in 70% of the patients by routine surveillance. This study also showed that patients with stage IV disease with a more frequent imaging surveillance had a better survival rate compared with those with a longer interval for surveillance, which was confirmed after correction for lead time bias.

Prospective studies that investigated the use, frequency, duration, and method of surveillance after surgery have not been performed. More importantly, there has been no study that investigated the use of intensive surveillance at all. Messager et al. reported a lack of consensus between practice and guidelines in ten European countries.⁶ In this relatively small geographical area, wide differences exist, some even within the same country. In some centers, only history and physical examination are performed, while in others tumor markers and CT scans are standard care. The frequency of visits varies between every 3 and 6 months.

Most retrospective studies conclude that routine postoperative surveillance after multimodal therapy will probably detect recurrent disease earlier when compared with symptom-triggered surveillance.^{7–9} The study from Lou shows that the yield rate of an upper endoscopy is very low, which is confirmed by Takeuchi et al.^{5,8} In all these studies, most recurrences were found by CT scans. PET/CT scan might even be more effective, although there is no evidence to support this. An important disadvantage of a PET scan is that it is even more expensive and is a higher burden to the patients, as they are in the hospital for several hours longer.

The ultimate goal of intensive surveillance is to improve prognosis by aggressive treatment of these recurrences. Whether this is achieved with intensive surveillance remains to be elucidated. If standard surveillance is considered, one should realize and discuss with the patient that, in the vast majority of cases, this only means that an asymptomatic recurrence is found several weeks earlier

before it would become symptomatic, and that the limited options for palliative treatment mean that the postoperative asymptomatic period has become shorter, with a very limited increase in survival. Although this might be difficult to discuss with the patient, the author's opinion is that it is important to do beforehand. In addition, the patient should be aware of potential findings of intensive imaging, for example, nonsignificant incidentalomas that might be accompanied with extra tests and biopsies and nonsymptomatic recurrent disease with no curative options, meaning that the patient has less time to live carefree with a good quality of life.

Ideally, surveillance should consist of a modality that is low in cost with low impact on hospital resources, low chance of finding irrelevant incidentalomas, and high negative and positive predictive value. In addition, an optimal surveillance interval should be determined to minimize incidence of symptomatic recurrence balanced with the lowest burden to the patient. Finally, a good surveillance program is only useful when there are good options for curative treatment of recurrent disease. It is evident that a lot of challenges remain to be tackled, but we should aim to keep working on this, since metastatic esophageal cancer is still a very aggressive disease with a 5-year survival rate of less than 5%.¹⁰

For the future, a large prospective randomized study should be performed in which a symptom-triggered group will be compared with an intensive surveillance group where different strategies and modalities will be compared. However, in such a study it might be difficult to include patients, as most patients would probably opt for intensive surveillance.¹¹ An alternative study design might be a stepped-wedge design.¹² With this study design, the new intensive surveillance group can be introduced step by step in all clinics and evaluated at the end of the study period. Another approach might be to set up a large international cohort and specifically compare the differences in surveillance with a propensity score matching analysis.

In conclusion, in the current era, symptom-triggered surveillance with a focus on functional complaints and quality of life is justified. When considering intensive surveillance, CT of the chest and abdomen is probably the most effective method. Upper endoscopy has a low yield rate and should only be performed with a specific indication. If intensive surveillance is broadly adopted, sufficient treatment options should be available and the extra cost and burden on the patient and the healthcare system should also be considered.

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